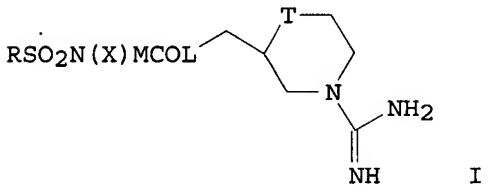
	AU 9179490	A1	19920109	AU 1991-79490	19910701 <--
	AU 650458	B2	19940623		
	HU 58288	A2	19920228	HU 1991-2206	19910701 <--
	HU 217815	B	20000428		
	JP 04230363	A2	19920819	JP 1991-185774	19910701 <--
	JP 07030022	B4	19950405		
	IL 98690	A1	19960514	IL 1991-98690	19910701 <--
	IL 112712	A1	19960912	IL 1991-112712	19910701 <--
	ES 2061125	T3	19941201	ES 1991-110928	19910702 <--
	NO 9102626	A	19920106	NO 1991-2626	19910704 <--
	NO 177704	B	19950731		
	NO 177704	C	19951108		
	FI 9103282	A	19920106	FI 1991-3282	19910705 <--
	US 5393760	A	19950228	US 1993-77476	19930615 <--
	US 5532232	A	19960702	US 1994-343168	19941122 <--
	US 5595999	A	19970121	US 1995-473060	19950607 <--
	US 5583133	A	19961210	US 1995-511428	19950804 <--
	FI 9601629	A	19960412	FI 1996-1629	19960412 <--
	US 5763436	A	19980609	US 1996-715038	19960917 <--
PRAI	CH 1990-2250	A	19900705		
	CH 1991-1315	A	19910502		
	US 1991-719429	A3	19910624		
	IL 1991-98690	A3	19910701		
	FI 1991-3282	A	19910705		
	US 1993-77476	A3	19930615		
	US 1994-343168	A3	19941122		
	US 1995-473060	A3	19950607		

OS MARPAT 116:214908

GI



I

AB Title compds. [I; R, R3 = (hetero)aryl, heterocyclyl; T = CH2, O; L = NH, O; N(X)M = N(SO2R3)CH2, (substituted) isoquinolinylene; X = H, CH2CO2H, alkoxycarbonylmethyl, alkyleneiminocarbonylmethyl, (alkylated) CH2CONH2; M = R1CH2CH, R1COCH2CH, PhCH2O2CNHCH2CH, etc.; R1 = (hetero)aryl, heterocyclyl, cycloalkyl], were prepd. Thus, tert-Bu R-4-hydroxymethyl-2,2-dimethyl-3-oxazolidinecarboxylate was successively tosylated, condensed with 2-indolinone using NaH in DMF, and treated with 2N HCl to give 1-[(R)-2-amino-3-hydroxypropyl]-2-indolinone. This was acylated with 2-naphthylsulfonyl chloride followed by Jones oxidn. to give N-(2-naphthylsulfonyl)-3-(2,3-dioxo-1-indolinyl)-D-alanine. This was converted to (R)-N-[(RS)-1-aminido-3-piperidinylmethyl]-.alpha.-(2-naphthylsulfonamido-2,3-dioxo-1-indolinepropionamide acetate. The latter inhibited thrombin with Ki = 8.55 nM and trypsin with Ki = 20,075.

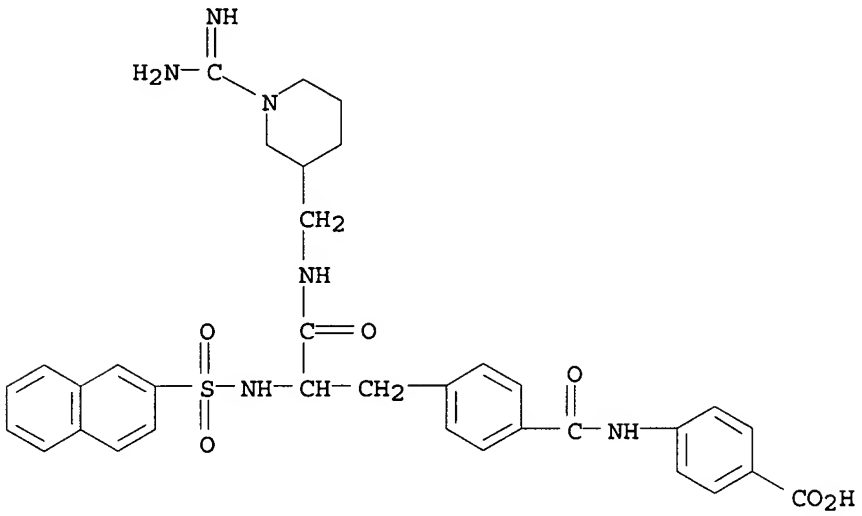
IT **140644-50-4P 140644-80-0P 140644-82-2P**
140644-84-4P 140644-86-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as antithrombotic)

RN 140644-50-4 CAPLUS

CN Benzoic acid, 4-[[4-[3-[[[1-(aminoiminomethyl)-3-piperidinyl]methyl]amino]-

2-[(2-naphthalenylsulfonyl)amino]-3-oxopropyl]benzoyl]amino]-,
monohydrochloride (9CI) (CA INDEX NAME)

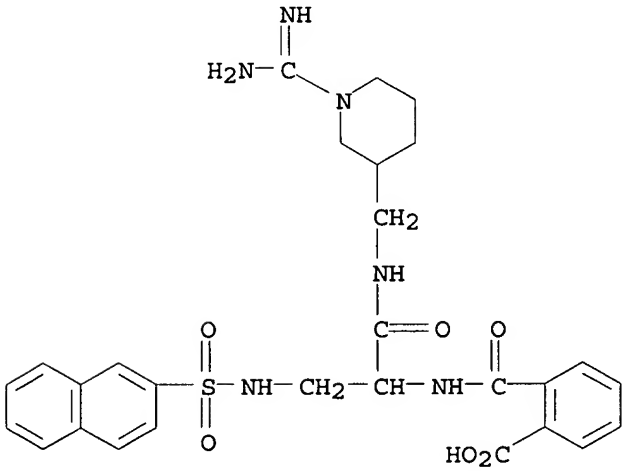
PAGE 1-A



PAGE 2-A

● HCl

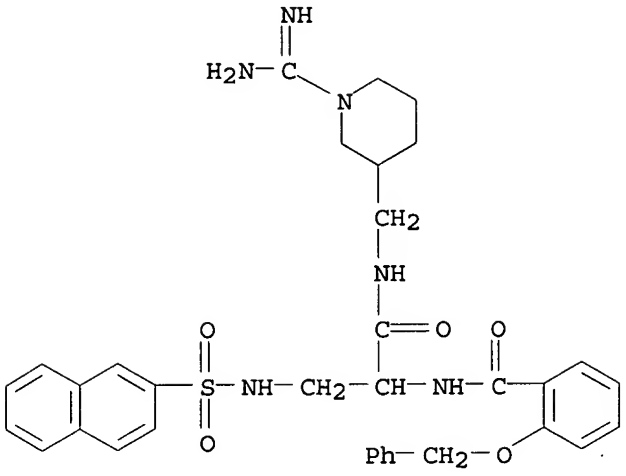
RN 140644-80-0 CAPLUS
CN Benzoic acid, 2-[[[2-[[[1-(aminoiminomethyl)-3-piperidinyl]methyl]amino]-1-[[(2-naphthalenylsulfonyl)amino]methyl]-2-oxoethyl]amino]carbonyl]- (9CI)
(CA INDEX NAME)



RN 140644-82-2 CAPLUS
CN Benzamide, N-[2-[[[1-(aminoiminomethyl)-3-piperidinyl]methyl]amino]-1-[[(2-naphthalenylsulfonyl)amino]methyl]-2-oxoethyl]-2-(phenylmethoxy)-,
monoacetate (9CI) (CA INDEX NAME)

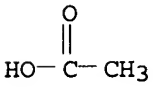
CM 1

CRN 140644-81-1
CMF C34 H38 N6 O5 S



CM 2

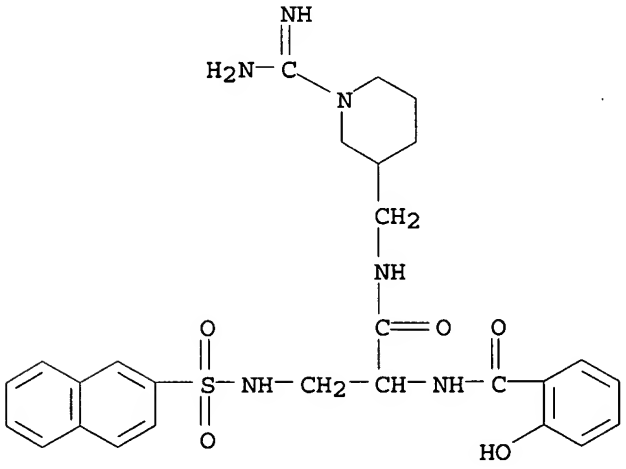
CRN 64-19-7
CMF C2 H4 O2



RN 140644-84-4 CAPLUS
CN Benzamide, N-[2-[[[1-(aminoiminomethyl)-3-piperidinyl]methyl]amino]-1-[[(2-naphthalenylsulfonyl)amino]methyl]-2-oxoethyl]-2-hydroxy-, monoacetate (salt) (9CI) (CA INDEX NAME)

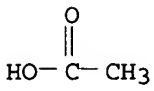
CM 1

CRN 140644-83-3
CMF C27 H32 N6 O5 S



CM 2

CRN 64-19-7
CMF C2 H4 O2

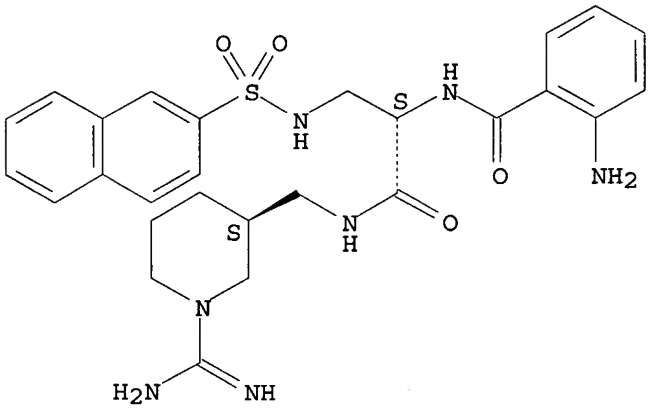


RN 140644-86-6 CAPLUS
CN Benzamide, 2-amino-N-[2-[[[1-(aminoiminomethyl)-3-piperidinyl]methyl]amino]-1-[[(2-naphthalenylsulfonyl)amino]methyl]-2-oxoethyl]-, [S-(R*,R*)]-, sulfite (2:1) (9CI) (CA INDEX NAME)

CM 1

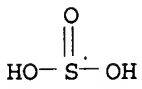
CRN 140644-85-5
CMF C27 H33 N7 O4 S

Absolute stereochemistry.



CM 2

CRN 7782-99-2
CMF H2 O3 S



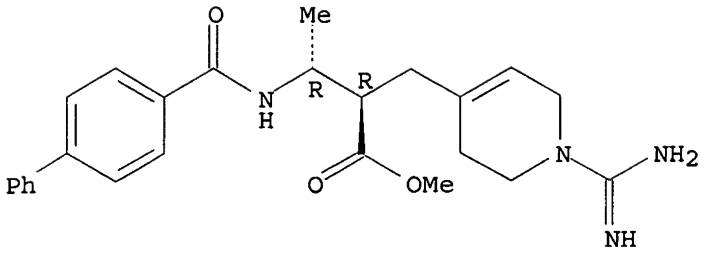
IT **140645-75-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for antithrombotic)
RN 140645-75-6 CAPLUS
CN Benzoic acid, 4-[[4-[3-[[[1-(aminoiminomethyl)-3-piperidinyl]methyl]amino]-2-[(2-naphthalenylsulfonyl)amino]-3-oxopropyl]benzoyl]amino]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

AN 1999:626174 CAPLUS
DN 131:243595
TI Preparation of piperidinyl and N-amidinopiperidinyl amino acid derivatives for inhibition of Factor Xa
IN Klein, Scott I.; Guertin, Kevin R.
PA Rhone-Poulenc Rorer Pharmaceuticals Inc., USA
SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9948870	A1	19990930	WO 1999-US6224	19990322
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2325471	AA	19990930	CA 1999-2325471	19990322
	AU 9931094	A1	19991018	AU 1999-31094	19990322
	EP 1080075	A1	20010307	EP 1999-912798	19990322
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	BR 9909086	A	20010904	BR 1999-9086	19990322
	JP 2002507600	T2	20020312	JP 2000-537853	19990322
	US 2002016339	A1	20020207	US 2001-922906	20010806
PRAI	US 1998-79002P	A2	19980323		
	US 1999-273618	A3	19990322		
	WO 1999-US6224	W	19990322		

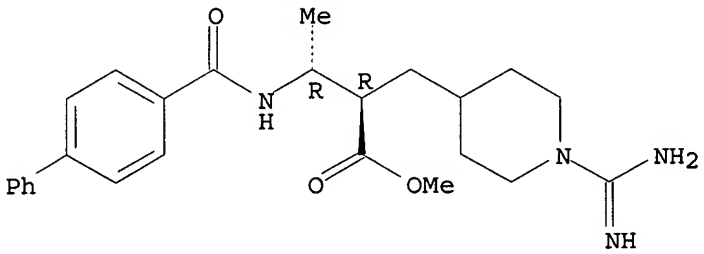
OS MARPAT 131:243595
AB Compds. R1R2CHCHR3NR7COR4 [R1 = (CH2CH2)mZ3, (CH:CH)mZ3, or (CH2)nZ3, where m = 1 or 2; n = 0, 1, or 3; Z3 = substituted aryl, cycloalkyl, or cycloalkenyl, (un)substituted heteroaryl, heterocyclyl, heterocyclenyl,etc.; R2 = H, CO2R5, COR5, CONR52, CH2OR6, CH2SR6, where R5 = H, alkyl; R6 = H, (un)substituted alkyl, acyl, aroyl, heteroaroyl; R3 = H, (un)substituted alkyl, (CH2CH2)oZ2, (CH:CH)oZ2, (CH2)pZ2, where o = 1 or 2; p = 0, 1, or 3; Z2 = (un)substituted aryl, heteroaryl, cycloalkyl, cycloalkenyl, heterocyclyl, or heterocyclenyl; R4 = alkyl, alkenyl, alkynyl, (un)substituted cycloalkyl, heterocyclyl, aryl, heteroaryl, etc.; R7 = H, alkyl] were prepd. for inhibiting the activity of Factor Xa. Thus, N-(4-phenylbenzoyl)-2-(R)-(1,2,5,6-tetrahydro-3-pyridylmethyl)-3-(R)-.beta.-alanine Me ester was prepd. via alkylation/acylation of N-(tert-butoxycarbonyl)-3(R)-.beta.-alanine Me ester.
IT **244267-06-9P 244267-08-1P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of piperidinyl and N-amidinopiperidinyl amino acid derivs. for inhibition of Factor Xa)
RN 244267-06-9 CAPLUS
CN 4-Pyridinepropanoic acid, 1-(aminoiminomethyl)-.alpha.-[(1R)-1-[([1,1'-biphenyl]-4-ylcarbonyl)amino]ethyl]-1,2,3,6-tetrahydro-, methyl ester, (.alpha.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 244267-08-1 CAPLUS
CN 4-Piperidinepropanoic acid, 1-(aminoiminomethyl)-.alpha.-[(1R)-1-[([1,1'-biphenyl]-4-ylcarbonyl)amino]ethyl]-, methyl ester, (.alpha.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN 1998:545398 CAPLUS
DN 129:161574
TI Preparation of [(N-amidinoazinyl)alkoxy]phenyl benzenesulfonates and analogs as protease inhibitors
IN Lu, Tianbao; Illig, Carl R.; Tomczuk, Bruce E.; Soll, Richard M.; Subasinghe, Nalin L.; Bone, Roger F.
PA 3-Dimensional Pharmaceuticals, Inc., USA
SO U.S., 43 pp., Cont.-in-part of U. S. Ser. No. 536,939, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5792769	A	19980811	US 1996-698401	19960815
	CA 2233344	AA	19970403	CA 1996-2233344	19960927
	WO 9711693	A1	19970403	WO 1996-US15609	19960927
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI				
	AU 9672012	A1	19970417	AU 1996-72012	19960927
	AU 714292	B2	19991223		
	EP 859607	A1	19980826	EP 1996-933186	19960927
	EP 859607	B1	20021218		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	BR 9610876	A	19990713	BR 1996-10876	19960927
	JP 11512722	T2	19991102	JP 1996-513732	19960927
	NZ 319474	A	20000128	NZ 1996-319474	19960927
	AT 229800	E	20030115	AT 1996-933186	19960927
	NO 9801393	A	19980525	NO 1998-1393	19980327
PRAI	US 1995-536939	B2	19950929		
	US 1996-698401	A	19960815		
	WO 1996-US15609	W	19960927		

OS MARPAT 129:161574
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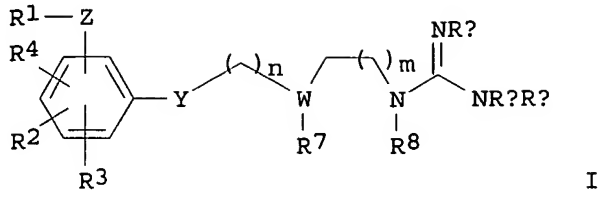

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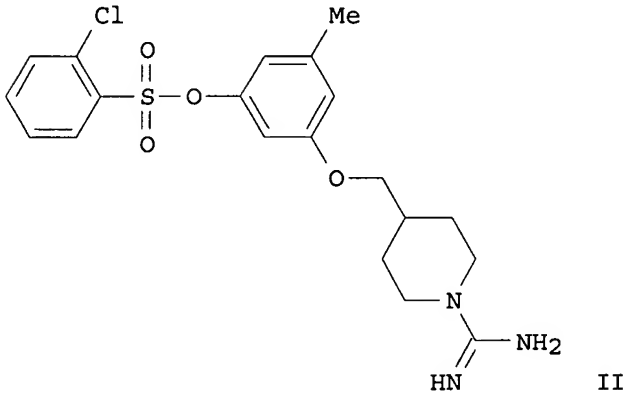


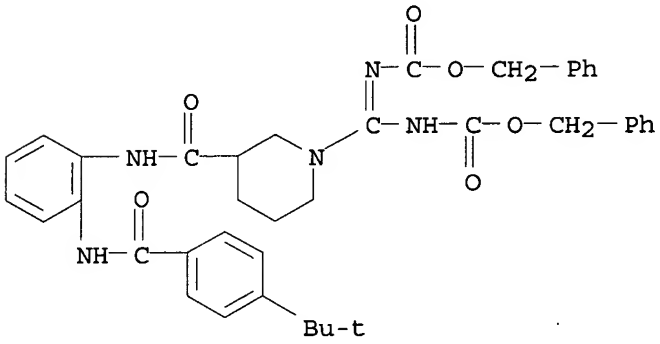
II

AB Title compds. I [R1 = (un)substituted alk(en/yn)yl, aryl(alkyl), (hetero)aryl, etc.; R2, R3, R4 = H, alky(en/yn)yl, cycloalkyl, aryl(alkyl), CF3, halo, cyano, CO2H or esters, etc.; or R2R3 = CH:CHCH:CH or (CH2)2-6; Z = NR10SO2, SO2O, NR10CO, CH2NR10, etc.; Y = bond, O, S, (un)substituted NH or CH2; W = N or (un)substituted CH; R7, R8 = H, alkyl, aryl(alkyl), hydroxyalkyl, carboxyalkyl; or R7R8 = bond, CH2, CH2CH2, with proviso; R10 = H, (alkoxy)alkyl, aryl(alkyl), etc.; Ra-Rc = H, OH, cyano, alkyl, alkoxy, aryloxy, etc.; m = 0-4; n = 0-8; with provisos] were prepd. For instance, orcinol underwent monoetherification with PhCH2Br (31%) and then esterification with 2-ClC6H4SO2Cl (88%) and hydrogenolysis (89%) to give 2-chlorobenzenesulfonic acid 3-hydroxy-5-methylphenyl ester. The latter was etherified with N-(tert-butoxycarbonyl)-4-**piperidinemethanol** using the Mitsunobu reaction (90%), followed by removal of the BOC group (95%) and guanidylation with aminoiminomethanesulfonic acid (36%), to give title compd. II. The latter inhibited human **thrombin** in vitro with a Ki of 0.008 .mu.M.

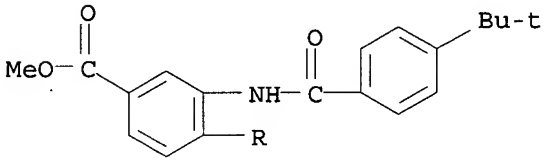
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

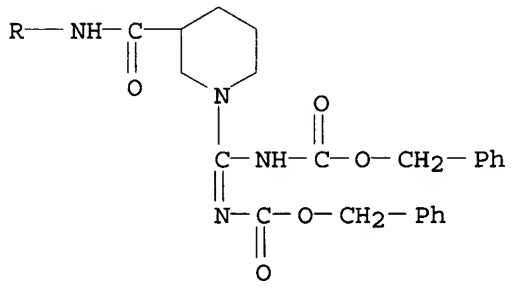
IT **219519-91-2P 219519-94-5P 219519-96-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(debenzyloxycarbonylation; prepn. of dibenzoylbenzenediamines as antithrombotic agents)

RN 219519-91-2 CAPLUS
CN Carbamic acid, [[3-[[[2-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]amino]carbonyl]-1-piperidinyl][[(phenylmethoxy)carbonyl]amino]methylene]-, phenylmethyl ester (9CI) (CA INDEX NAME)

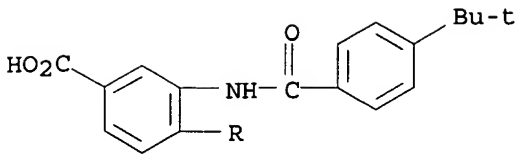


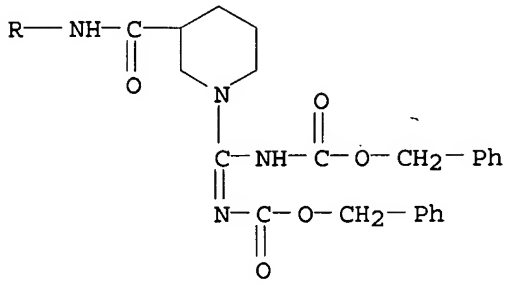
RN 219519-94-5 CAPLUS
CN Benzoic acid, 3-[[4-(1,1-dimethylethyl)benzoyl]amino]-4-[[[1-[[[(phenylmethoxy)carbonyl]amino][[(phenylmethoxy)carbonyl]imino]methyl]-3-piperidinyl]carbonyl]amino]-, methyl ester (9CI) (CA INDEX NAME)





RN 219519-96-7 CAPLUS
CN Benzoic acid, 3-[[4-(1,1-dimethylethyl)benzoyl]amino]-4-[[[1-[[[(phenylmethoxy)carbonyl]amino][[(phenylmethoxy)carbonyl]imino]methyl]-3-piperidinyl]carbonyl]amino]- (9CI) (CA INDEX NAME)





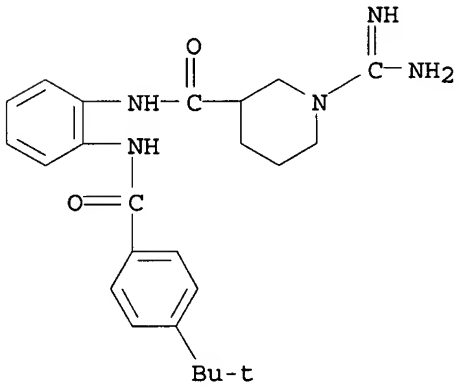
IT **219519-93-4P 219519-95-6P 219519-97-8P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of dibenzoylbenzenediamines as antithrombotic agents)

RN 219519-93-4 CAPLUS

CN 3-Piperidinecarboxamide, 1-(aminoiminomethyl)-N-[2-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

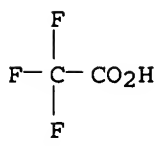
CM 1

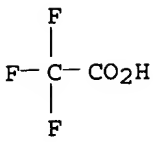
CRN 219519-92-3
CMF C24 H31 N5 O2



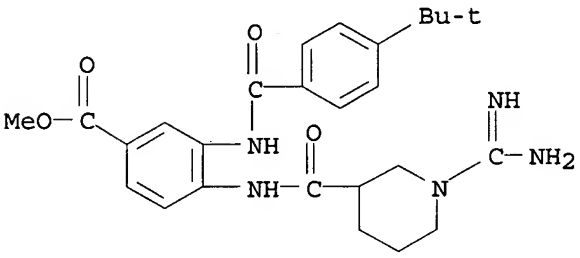
CM 2

CRN 76-05-1
CMF C2 H F3 O2



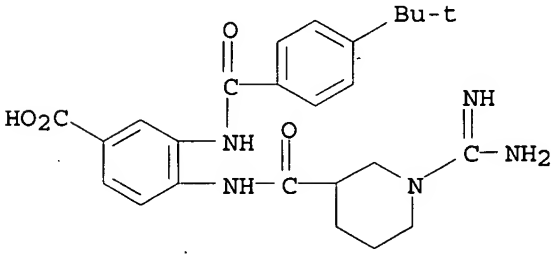


RN 219519-95-6 CAPLUS
CN Benzoic acid, 4-[[[1-(aminoiminomethyl)-3-piperidinyl]carbonyl]amino]-3-[[4-(1,1-dimethylethyl)benzoyl]amino]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



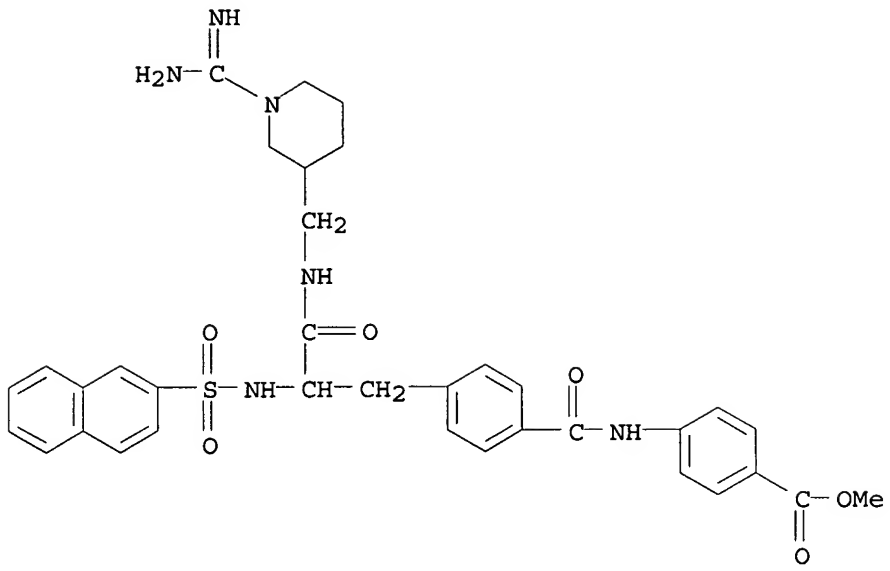
● HCl

RN 219519-97-8 CAPLUS
CN Benzoic acid, 4-[[[1-(aminoiminomethyl)-3-piperidinyl]carbonyl]amino]-3-[[4-(1,1-dimethylethyl)benzoyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

PAGE 1-A



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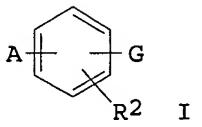
● HCl

L16 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2003 ACS
AN 1991:492947 CAPLUS
DN 115:92947
TI Preparation of N-amidobenzoyl-.beta.-alanines and analogs as fibrinogen antagonists and antitumor agents
IN Alig, Leo; Edenhofer, Albrecht; Mueller, Marcel; Trzeciak, Arnold; Weller, Thomas
PA Hoffmann-La Roche, F., und Co. A.-G., Switz.
SO Eur. Pat. Appl., 28 pp.
CODEN: EPXXDW
DT **Patent**
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 372486	A2	19900613	EP 1989-122396	19891205 <--
	EP 372486	A3	19910612		
	EP 372486	B1	19940601		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	US 5039805	A	19910813	US 1989-440949	19891124 <--
	CA 2004127	AA	19900608	CA 1989-2004127	19891129 <--
	ZA 8909210	A	19900829	ZA 1989-9210	19891201 <--
	IL 92518	A1	19941129	IL 1989-92518	19891201 <--
	HU 53068	A2	19900928	HU 1989-6350	19891204 <--
	HU 206192	B	19920928		
	AU 8945865	A1	19901101	AU 1989-45865	19891204 <--
	AU 648751	B2	19940505		
	AT 106389	E	19940615	AT 1989-122396	19891205 <--
	ES 2054995	T3	19940816	ES 1989-122396	19891205 <--
	DK 8906153	A	19900609	DK 1989-6153	19891206 <--
	DK 171888	B1	19970804		
	NO 8904919	A	19900611	NO 1989-4919	19891207 <--
	JP 02223543	A2	19900905	JP 1989-320391	19891208 <--

JP 06010179 B4 19940209
PRAI CH 1988-4543 19881208
CH 1989-3703 19891011
EP 1989-122396 19891205
OS MARPAT 115:92947
GI



I

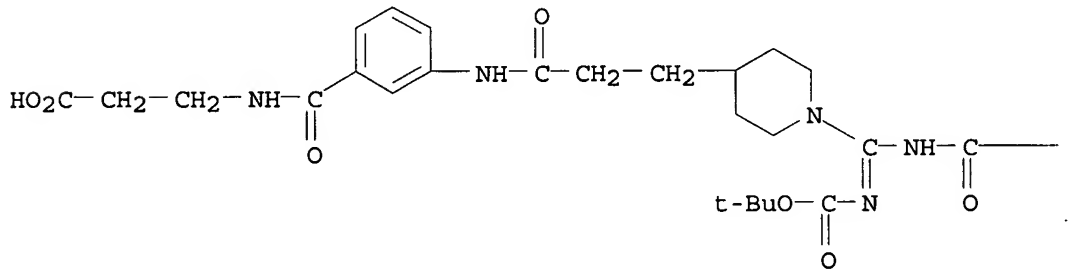
AB The title compds. [I; A = R1CONH(CH2)i; G = (CH2)jCONHCHR1CH2CO2H; R1 = CHRa(CH2)nNHR6, T1C6H4CH2NHRc, TmC6H4(NH)pC(:NH)NH2, aminomethylcyclohexyl, etc.; Ra = H, NH2, alkoxycarbonylamino, NHCO2CH2Ph, NHCOCH2NYCH2CH2NHY; R6 = H, amidino, C(:NH)(CH2)hMe; Rc = H, amidino; R2 = H, me, OMe, NO2, halo, etc.; R3 = H, CONH2, CORf, CO2Rg; Rf= N-linked amino acid residue; Rg = H, alkyl; T = CH2, CH:CH, CHRdCH2; Rd = groups cited for Ra, NHBz, NHCOC6H4N3, arylsulfonylamino; Y = H, CO2CMe3, CO2CH2Ph; i, j, l, m, p = 0,1; k = 0-3; n = 1-6] were prepd. Thus, RCl [R = 4-[H2N(HN:)C]C6H4CO] was condensed with 3-(R4HN)C6H4CONHCH2CH2CO2R5 (II; R4 = H, R5 = CH2Ph) to give, after hydrogenolysis, II (R4 = R, R5 = H) which had IC50 of 10-4 .mu.M against fibrinogen binding to glycoprotein IIb/IIIa.

IT **135322-11-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, in prepn. of antitumor agents and fibrinogen antagonists)

RN 135322-11-1 CAPLUS

CN .beta.-Alanine, N-[3-[[3-[1-[[[(1,1-dimethylethoxy)carbonyl]amino][[(1,1-dimethylethoxy)carbonyl]imino]methyl]-4-piperidinyl]-1-oxopropyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

—OBu-t

IT **135321-08-3P 135321-11-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of, as antitumor agent and fibrinogen antagonist)

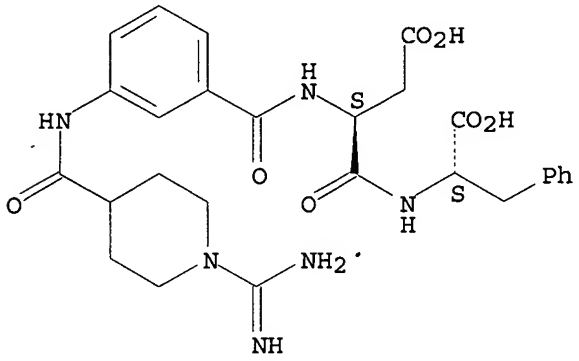
RN 135321-08-3 CAPLUS

CN L-Phenylalanine, N-[N-[3-[[[1-(aminoiminomethyl)-4-piperidinyl]carbonyl]amino]benzoyl]-L-.alpha.-aspartyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

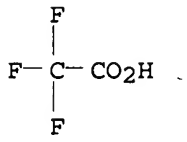
CRN 135321-07-2
CMF C27 H32 N6 O7

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

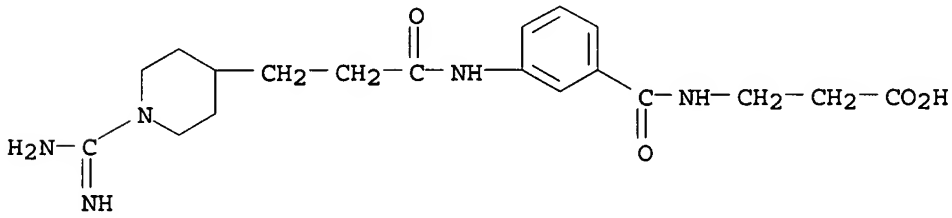


RN 135321-11-8 CAPLUS

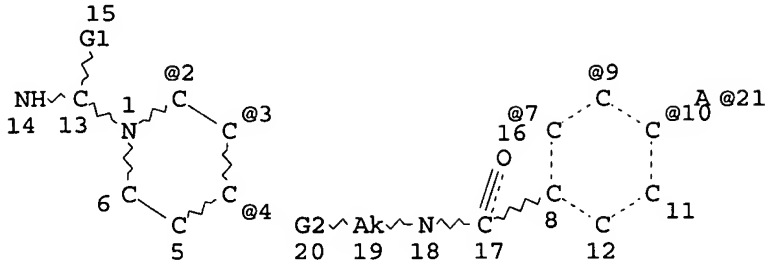
CN .beta.-Alanine, N-[3-[[3-[1-(aminoiminomethyl)-4-piperidinyl]-1-oxopropyl]amino]benzoyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 135321-10-7
CMF C19 H27 N5 O4



=> d 18
L8 HAS NO ANSWERS
L8 STR



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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 4 8
NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE

=> search l8
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ENTER SCOPE OF SEARCH (SAMPLE), FULL, RANGE, OR SUBSET:subset
ENTER SUBSET L# OR (END):13
ENTER SUBSET SEARCH SCOPE - SAMPLE, FULL, RANGE, OR (END):ful
FULL SUBSET SEARCH INITIATED 17:31:58 FILE 'REGISTRY'
FULL SUBSET SCREEN SEARCH COMPLETED - 269 TO ITERATE

100.0% PROCESSED 269 ITERATIONS 20 ANSWERS
SEARCH TIME: 00.00.01

L9 20 SEA SUB=L3 SSS FUL L8

=> fil caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	36.10	235.93

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-11.72

FILE 'CAPLUS' ENTERED AT 17:32:11 ON 14 APR 2003

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FILE COVERS 1907 - 14 Apr 2003 VOL 138 ISS 16
FILE LAST UPDATED: 13 Apr 2003 (20030413/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l9
L10 2 L9

L10 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS
AN 2002:449651 CAPLUS
DN 137:20300
TI Preparation of guanidines and amidines as Factor Xa and/or VIIa inhibitors.
IN Peyman, Anuschirwan; Will, David William; Gerlach, Uwe; Nazare, Marc; Zoller, Gerhard; Nestler, Hans-Peter; Matter, Hans; Al-Obeidi, Fahad
PA Aventis Pharma Deutschland G.m.b.H., Germany
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002046159	A1	20020613	WO 2001-EP13874	20011128
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002033206	A5	20020618	AU 2002-33206	20011128
	US 2002173656	A1	20021121	US 2001-4422	20011206
PRAI	EP 2000-126750	A	20001206		
	WO 2001-EP13874	W	20011128		

OS MARPAT 137:20300
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS
AN 1999:365690 CAPLUS
DN 131:44660
TI Preparation of biphenylamidine derivatives as factor Xa inhibitors and anticoagulants containing them
IN Nakata, Tomohisa; Hara, Takayuki; Takano, Yasunobu; Sugiura, Satoshi; Tsutsumi, Takaharu; Takasawa, Haruji; Takarada, Reiko
PA Teijin Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 31 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

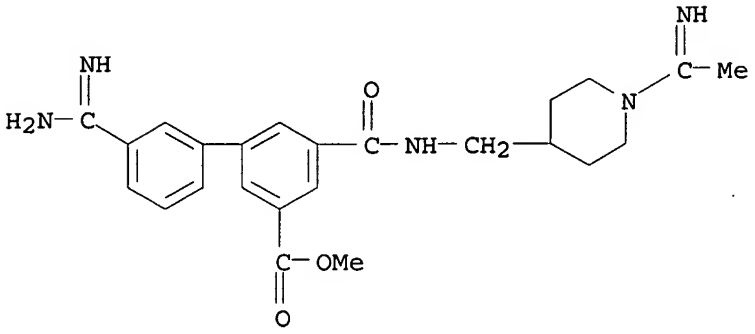
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 11152269	A2	19990608	JP 1997-319697	19971120
PRAI	JP 1997-319697		19971120		

OS MARPAT 131:44660

=> d hitstr 2

L10 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS
IT **227474-39-7P 227474-49-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of biphenylamidine derivs. as factor Xa inhibitors)

RN 227474-39-7 CAPLUS
CN [1,1'-Biphenyl]-3-carboxylic acid, 3'-(aminoiminomethyl)-5-[[[[1-(1-iminoethyl)-4-piperidinyl]methyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



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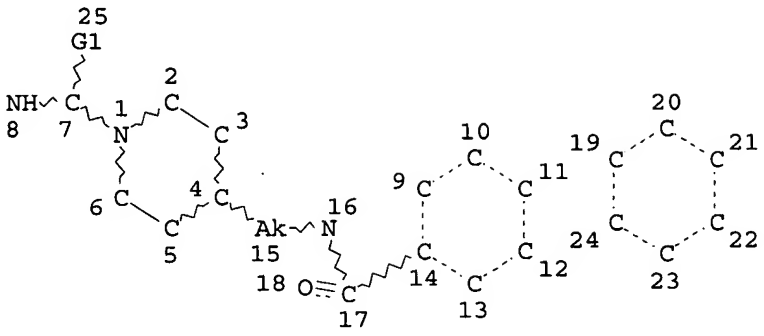

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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 1 14 19
NUMBER OF NODES IS 25

STEREO ATTRIBUTES: NONE

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FULL SCREEN SEARCH COMPLETED - 2577 TO ITERATE

100.0% PROCESSED 2577 ITERATIONS 22 ANSWERS
SEARCH TIME: 00.00.01

L5 22 SEA SSS FUL L3

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	150.95	151.16

FILE 'CAPLUS' ENTERED AT 16:31:55 ON 14 APR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 14 Apr 2003 VOL 138 ISS 16
FILE LAST UPDATED: 13 Apr 2003 (20030413/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l5
L6 3 L5

=> d bib abs 1-3

L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS
AN 2002:449651 CAPLUS
DN 137:20300
TI Preparation of guanidines and amidines as Factor Xa and/or VIIa inhibitors.
IN Peyman, Anuschirwan; Will, David William; Gerlach, Uwe; Nazare, Marc; Zoller, Gerhard; Nestler, Hans-Peter; Matter, Hans; Al-Obeidi, Fahad
PA Aventis Pharma Deutschland G.m.b.H., Germany
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002046159	A1	20020613	WO 2001-EP13874	20011128
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002033206	A5	20020618	AU 2002-33206	20011128
	US 2002173656	A1	20021121	US 2001-4422	20011206
PRAI	EP 2000-126750	A	20001206		
	WO 2001-EP13874	W	20011128		

OS MARPAT 137:20300
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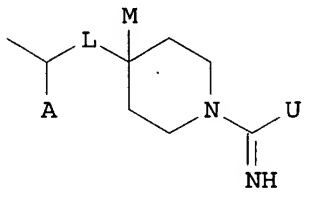
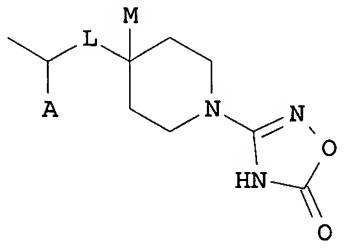
Q1 = 

Q2 = 

AB R0QXQ1DCONR10V [R0 = (substituted) Ph, heteroaryl contg. 1-2 N atoms; Q, Q1 = bond, O, S, NR10, CONR10, SO, SO2, CO, SO2NR10; R10 = H, alkyl; X = bond, (substituted) alkylene, cycloalkylene; D = mono- , bicyclic aryl, heterocyclyl, pyridyl; V = Q1, Q2, etc.; A = H, CO2H, (substituted) alkoxycarbonyl, etc.; L = bons, (substituted) alkylene; U = NH2, alkyl, alkoxycarbonylamino, etc.; M = H, alkyl, OH], were prepd. Thus,

4-Bromo-N-(1-carbamimidoylpiperidin-4-ylmethyl)-3-[2-(2,4-dichlorophenyl)ethoxy]-5-hydroxybenzamide (I), prepd. by solid phase synthesis, inhibited Factor Xa with Ki = 0.0137 .mu.M.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS
AN 1999:626174 CAPLUS
DN 131:243595
TI Preparation of piperidinyl and N-amidinopiperidinyl amino acid derivatives for inhibition of Factor Xa
IN Klein, Scott I.; Guertin, Kevin R.
PA Rhone-Poulenc Rorer Pharmaceuticals Inc., USA
SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9948870	A1	19990930	WO 1999-US6224	19990322
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2325471	AA	19990930	CA 1999-2325471	19990322
AU 9931094	A1	19991018	AU 1999-31094	19990322
EP 1080075	A1	20010307	EP 1999-912798	19990322
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
BR 9909086	A	20010904	BR 1999-9086	19990322
JP 2002507600	T2	20020312	JP 2000-537853	19990322
US 2002016339	A1	20020207	US 2001-922906	20010806
PRAI US 1998-79002P	A2	19980323		
US 1999-273618	A3	19990322		
WO 1999-US6224	W	19990322		

OS MARPAT 131:243595
AB Compds. R1R2CHCHR3NR7COR4 [R1 = (CH2CH2)mZ3, (CH:CH)mZ3, or (CH2)nZ3, where m = 1 or 2; n = 0, 1, or 3; Z3 = substituted aryl, cycloalkyl, or cycloalkenyl, (un)substituted heteroaryl, heterocyclyl, heterocyclenyl,etc.; R2 = H, CO2R5, COR5, CONR52, CH2OR6, CH2SR6, where R5 = H, alkyl; R6 = H, (un)substituted alkyl, acyl, aroyl, heteroaroyl; R3 = H, (un)substituted alkyl, (CH2CH2)oZ2, (CH:CH)oZ2, (CH2)pZ2, where o = 1 or 2; p = 0, 1, or 3; Z2 = (un)substituted aryl, heteroaryl, cycloalkyl, cycloalkenyl, heterocyclyl, or heterocyclenyl; R4 = alkyl, alkenyl, alkynyl, (un)substituted cycloalkyl, heterocyclyl, aryl, heteroaryl, etc.; R7 = H, alkyl] were prepd. for inhibiting the activity of Factor Xa. Thus, N-(4-phenylbenzoyl)-2-(R)-(1,2,5,6-tetrahydro-3-pyridylmethyl)-3-(R)-.beta.-alanine Me ester was prepd. via alkylation/acylation of N-(tert-butoxycarbonyl)-3(R)-.beta.-alanine Me ester.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS
AN 1999:365690 CAPLUS
DN 131:44660
TI Preparation of biphenylamidine derivatives as factor Xa inhibitors and anticoagulants containing them
IN Nakata, Tomohisa; Hara, Takayuki; Takano, Yasunobu; Sugiura, Satoshi; Tsutsumi, Takaharu; Takasawa, Haruji; Takarada, Reiko

PA Teijin Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 31 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 11152269	A2	19990608	JP 1997-319697	19971120
PRAI	JP 1997-319697		19971120		

OS MARPAT 131:44660
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

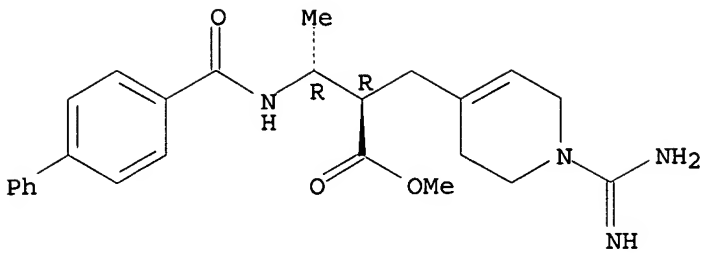
AB The title derivs. I [A = amidino in which one N atom may be substituted with OH, NH2, C1-8 alkyl, aryl, aralkyl, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl; R1 = H, F, Cl, Br, NH2, NO2, C1-8 alkyl, C1-8 alkoxy; L = direct bond, C1-4 alkylene; R2 = H, F, Cl, Br, OH, NH2, C1-8 alkoxy, CO2H, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, carbamoyl which may be substituted with 1-2 C1-8 alkyl or in which N may be derived from amino acid residue, C1-8 alkylcarbonyl, alkylsulfenyl, alkylsulfinyl, alkylsulfonyl, mono- or di-C1-8 alkyl-amino, mono- or di-C1-8 alkylaminosulfonyl, SO3H, phosphono, bis(hydroxycarbonyl)methyl, bis(alkoxycarbonyl)methyl, 5-tetrazolyl; R3 = H, F, Cl, Br, OH, NH2, NO2, C1-8 alkyl, CO2H, alkoxycarbonyl; n = 0-3; X = O, S, SO, SO2, NHCONH, NR4, CONR5, NR5CO, NR5SO2, SO2NR5 (R4 = H, C1-10 alkyl, C1-10 alkylcarbonyl, C1-10 alkylsulfonyl; R5 = H, C1-10 alkyl; alkyl in R4 and R5 may be substituted with aryl, OH, NH2, halo, C1-8 alkoxy, CO2H, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, carbamoyl which may be substituted with 1-2 C1-8 alkyl or in which N may be derived from amino acid residue, 5-tetrazolyl); Y = C4-8 cycloalkyl, adamantyl (CH2 of these ring may be replaced by CO or may be substituted), heterocyclyl Q (5-8 member), Q1 (6-8 member), Q2 (6-8 member) (substituents of the rings are defined)] and their pharmaceutically acce. Also claimed are anticoagulants or prophylactic and therapeutic drugs contg. I or their salts and excipients. Me 3-(3-amidinophenyl)-5-[2-(1-acetimidoyl-4-piperidyl)ethylamino]benzoate (II) was prepd. from Me 3-amino-5-hydroxybenzoate via Me 3-(tert-butoxycarbonyl)amino-5-hydroxybenzoate, Me 3-(tert-butoxycarbonyl)amino-5-(trifluoromethanesulfonyl)oxybenzoate, Me 3-(3-cyanophenyl)-5-(tert-butoxycarbonyl)aminobenzoate, Me 3-(3-cyanophenyl)-5-aminobenzoate, Me 3-(3-cyanophenyl)-5-[2-(1-tert-butoxycarbonyl-4-piperidyl)ethylamino]benzoate, and Me 3-(3-amidinophenyl)-5-[2-(4-piperidyl)ethylamino]benzoate. IC50 of II against factor Xa was 0.1-10 .mu.M.

AN 1999:626174 CAPLUS
DN 131:243595
TI Preparation of piperidinyl and N-amidinopiperidinyl amino acid derivatives for inhibition of Factor Xa
IN Klein, Scott I.; Guertin, Kevin R.
PA Rhone-Poulenc Rorer Pharmaceuticals Inc., USA
SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9948870	A1	19990930	WO 1999-US6224	19990322
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2325471	AA	19990930	CA 1999-2325471	19990322
	AU 9931094	A1	19991018	AU 1999-31094	19990322
	EP 1080075	A1	20010307	EP 1999-912798	19990322
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	BR 9909086	A	20010904	BR 1999-9086	19990322
	JP 2002507600	T2	20020312	JP 2000-537853	19990322
	US 2002016339	A1	20020207	US 2001-922906	20010806
PRAI	US 1998-79002P	A2	19980323		
	US 1999-273618	A3	19990322		
	WO 1999-US6224	W	19990322		

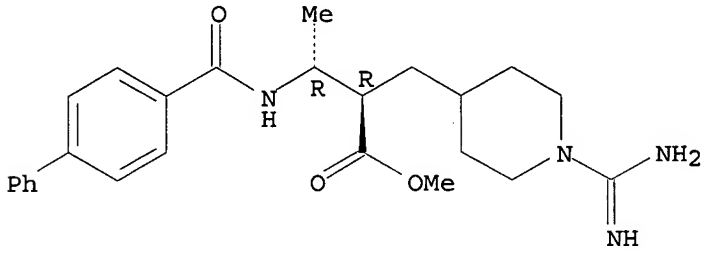
OS MARPAT 131:243595
AB Compds. R1R2CHCHR3NR7COR4 [R1 = (CH2CH2)mZ3, (CH:CH)mZ3, or (CH2)nZ3, where m = 1 or 2; n = 0, 1, or 3; Z3 = substituted aryl, cycloalkyl, or cycloalkenyl, (un)substituted heteroaryl, heterocyclyl, heterocyclenyl,etc.; R2 = H, CO2R5, COR5, CONR52, CH2OR6, CH2SR6, where R5 = H, alkyl; R6 = H, (un)substituted alkyl, acyl, aroyl, heteroaroyl; R3 = H, (un)substituted alkyl, (CH2CH2)oZ2, (CH:CH)oZ2, (CH2)pZ2, where o = 1 or 2; p = 0, 1, or 3; Z2 = (un)substituted aryl, heteroaryl, cycloalkyl, cycloalkenyl, heterocyclyl, or heterocyclenyl; R4 = alkyl, alkenyl, alkynyl, (un)substituted cycloalkyl, heterocyclyl, aryl, heteroaryl, etc.; R7 = H, alkyl] were prepd. for inhibiting the activity of Factor Xa. Thus, N-(4-phenylbenzoyl)-2-(R)-(1,2,5,6-tetrahydro-3-pyridylmethyl)-3-(R)-.beta.-alanine Me ester was prepd. via alkylation/acylation of N-(tert-butoxycarbonyl)-3(R)-.beta.-alanine Me ester.
IT **244267-06-9P 244267-08-1P 244267-12-7P**
244267-15-0P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of piperidinyl and N-amidinopiperidinyl amino acid derivs. for inhibition of Factor Xa)
RN 244267-06-9 CAPLUS
CN 4-Pyridinepropanoic acid, 1-(aminoiminomethyl)-.alpha.-[(1R)-1-[([1,1'-biphenyl]-4-ylcarbonyl)amino]ethyl]-1,2,3,6-tetrahydro-, methyl ester, (.alpha.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



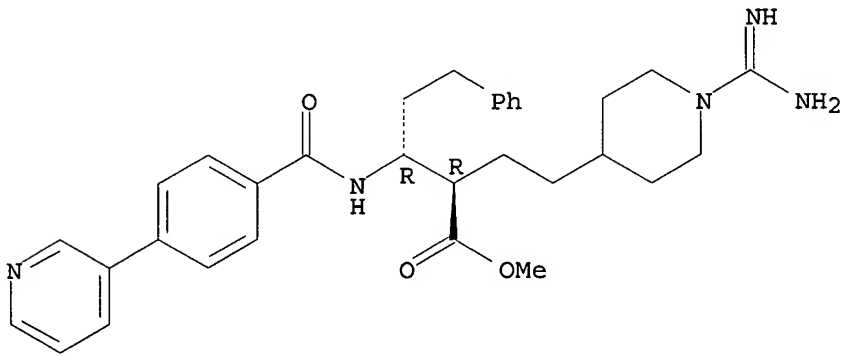
RN 244267-08-1 CAPLUS
CN 4-Piperidinepropanoic acid, 1-(aminoiminomethyl)-.alpha.-[(1R)-1-[([1,1'-biphenyl]-4-ylcarbonyl)amino]ethyl]-, methyl ester, (.alpha.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



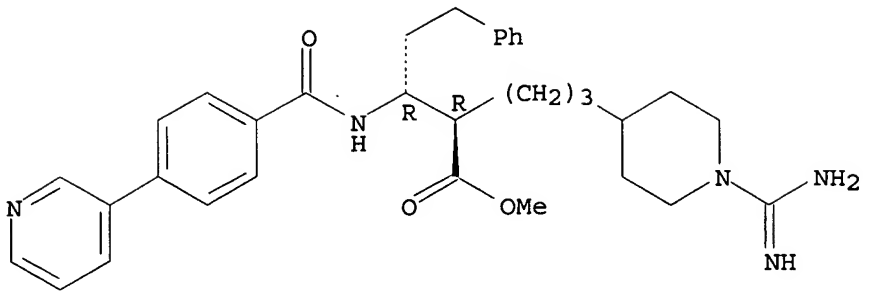
RN 244267-12-7 CAPLUS
CN 4-Piperidinebutanoic acid, 1-(aminoiminomethyl)-.alpha.-[(1R)-3-phenyl-1-[[4-(3-pyridinyl)benzoyl]amino]propyl]-, methyl ester, (.alpha.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 244267-15-0 CAPLUS
CN 4-Piperidinepentanoic acid, 1-(aminoiminomethyl)-.alpha.-[(1R)-3-phenyl-1-[[4-(3-pyridinyl)benzoyl]amino]propyl]-, methyl ester, (.alpha.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN 1999:365690 CAPLUS
DN 131:44660
TI Preparation of biphenylamidine derivatives as factor Xa inhibitors and anticoagulants containing them
IN Nakata, Tomohisa; Hara, Takayuki; Takano, Yasunobu; Sugiura, Satoshi; Tsutsumi, Takaharu; Takasawa, Haruji; Takarada, Reiko
PA Teijin Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 31 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 11152269	A2	19990608	JP 1997-319697	19971120
PRAI	JP 1997-319697		19971120		

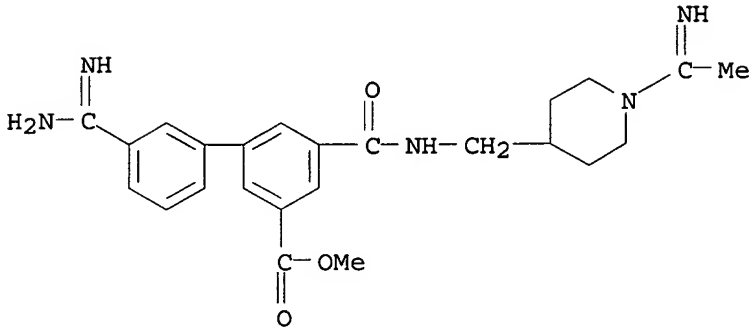
OS MARPAT 131:44660
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

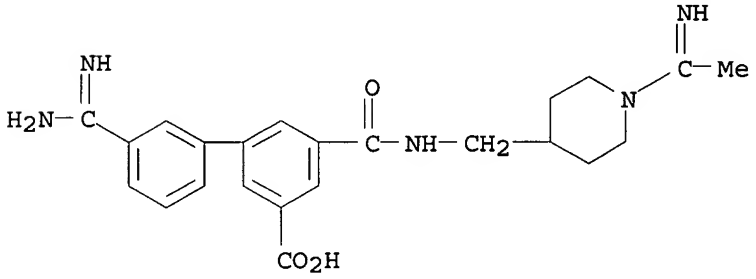
AB The title derivs. I [A = amidino in which one N atom may be substituted with OH, NH2, C1-8 alkyl, aryl, aralkyl, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl; R1 = H, F, Cl, Br, NH2, NO2, C1-8 alkyl, C1-8 alkoxy; L = direct bond, C1-4 alkylene; R2 = H, F, Cl, Br, OH, NH2, C1-8 alkoxy, CO2H, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, carbamoyl which may be substituted with 1-2 C1-8 alkyl or in which N may be derived from amino acid residue, C1-8 alkylcarbonyl, alkylsulfenyl, alkylsulfinyl, alkylsulfonyl, mono- or di-C1-8 alkyl-amino, mono- or di-C1-8 alkylaminosulfonyl, SO3H, phosphono, bis(hydroxycarbonyl)methyl, bis(alkoxycarbonyl)methyl, 5-tetrazolyl; R3 = H, F, Cl, Br, OH, NH2, NO2, C1-8 alkyl, CO2H, alkoxycarbonyl; n = 0-3; X = O, S, SO, SO2, NHCONH, NR4, CONR5, NR5CO, NR5SO2, SO2NR5 (R4 = H, C1-10 alkyl, C1-10 alkylcarbonyl, C1-10 alkylsulfonyl; R5 = H, C1-10 alkyl; alkyl in R4 and R5 may be substituted with aryl, OH, NH2, halo, C1-8 alkoxy, CO2H, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, carbamoyl which may be substituted with 1-2 C1-8 alkyl or in which N may be derived from amino acid residue, 5-tetrazolyl); Y = C4-8 cycloalkyl, adamantyl (CH2 of these ring may be replaced by CO or may be substituted), heterocyclyl Q (5-8 member), Q1 (6-8 member), Q2 (6-8 member) (substituents of the rings are defined)] and their pharmaceutically acce. Also claimed are anticoagulants or prophylactic and therapeutic drugs contg. I or their salts and excipients. Me 3-(3-amidinophenyl)-5-[2-(1-acetimidoyl-4-piperidyl)ethylamino]benzoate (II) was prepd. from Me 3-amino-5-hydroxybenzoate via Me 3-(tert-butoxycarbonyl)amino-5-hydroxybenzoate, Me 3-(tert-butoxycarbonyl)amino-5-(trifluoromethanesulfonyl)oxybenzoate, Me 3-(3-cyanophenyl)-5-(tert-butoxycarbonyl)aminobenzoate, Me 3-(3-cyanophenyl)-5-aminobenzoate, Me 3-(3-cyanophenyl)-5-[2-(1-tert-butoxycarbonyl-4-piperidyl)ethylamino]benzoate, and Me 3-(3-amidinophenyl)-5-[2-(4-piperidyl)ethylamino]benzoate. IC50 of II against factor Xa was 0.1-10 .mu.M.

IT **227474-39-7P 227474-49-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of biphenylamidine derivs. as factor Xa inhibitors)
RN 227474-39-7 CAPLUS

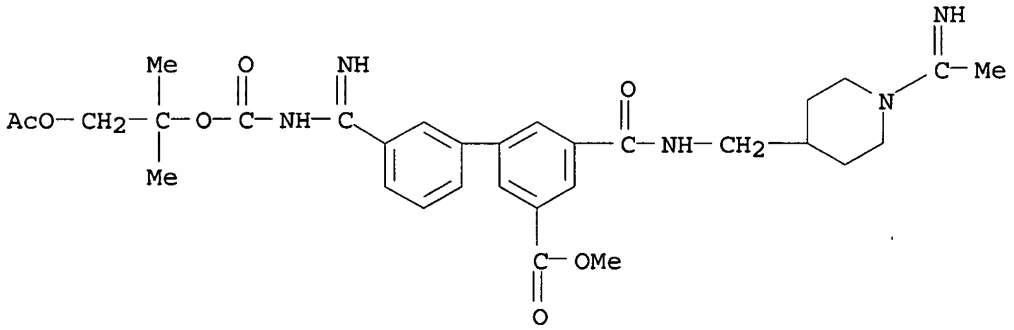
CN [1,1'-Biphenyl]-3-carboxylic acid, 3'-(aminoiminomethyl)-5-[[[[1-(1-iminoethyl)-4-piperidinyl]methyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 227474-49-9 CAPLUS
CN [1,1'-Biphenyl]-3-carboxylic acid, 3'-(aminoiminomethyl)-5-[[[[1-(1-iminoethyl)-4-piperidinyl]methyl]amino]carbonyl]- (9CI) (CA INDEX NAME)

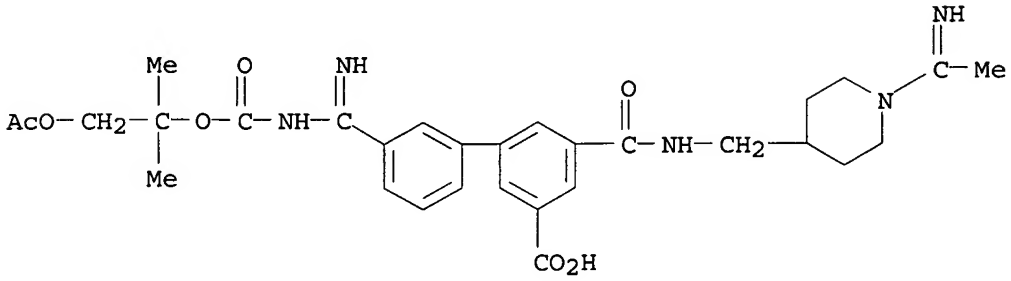


IT **227474-61-5P 227474-63-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of biphenylamidine derivs. as factor Xa inhibitors)
RN 227474-61-5 CAPLUS
CN [1,1'-Biphenyl]-3-carboxylic acid, 3'-[[[[2-(acetyloxy)-1,1-dimethylethoxy]carbonyl]amino]iminomethyl]-5-[[[[1-(1-iminoethyl)-4-piperidinyl]methyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



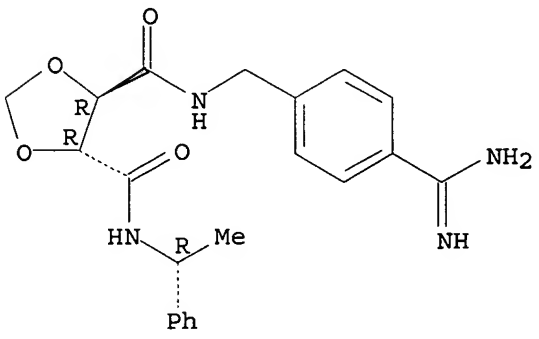
RN 227474-63-7 CAPLUS
CN [1,1'-Biphenyl]-3-carboxylic acid, 3'-[[[[2-(acetyloxy)-1,1-

dimethylethoxy]carbonyl]amino]iminomethyl]-5-[[[[1-(1-iminoethyl)-4-piperidinyl]methyl]amino]carbonyl]- (9CI) (CA INDEX NAME)



AN 2001:150305 CAPLUS
DN 135:15886
TI Computational modelling of inhibitor binding to human thrombin
AU Ljungberg, K. B.; Marelius, J.; Musil, D.; Svensson, P.; Norden, B.; Aqvist, J.
CS BMC, Department of Cell and Molecular Biology, Uppsala University, Uppsala, SE-751 24, Swed.
SO European Journal of Pharmaceutical Sciences (2001), 12(4), 441-446
CODEN: EPSCED; ISSN: 0928-0987
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
AB Thrombin is an essential protein involved in blood clot formation and an important clin. target, since disturbances of the coagulation process cause serious cardiovascular diseases such as thrombosis. Here the authors evaluate the performance of a mol. dynamics based method for predicting the binding affinities of different types of human thrombin inhibitors. For a series of eight ligands, the method ranks their relative affinities reasonably well. The binding free energy difference between high and low affinity representatives in the test set is quant. reproduced, as well as the stereospecificity for a chiral inhibitor. The original parametrization of this linear interaction energy method requires the addn. of a const. energy term in the case of thrombin. This yields a mean unsigned error of 0.68 kcal/mol for the abs. binding free energies. This type of approach is also useful for elucidating three-dimensional structure-activity relationships in terms of microscopic interactions of the ligands with the solvated enzyme.
IT **342632-27-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)
(computational modeling of benzamidine deriv. inhibitors binding to human thrombin)
RN 342632-27-3 CAPLUS
CN 1,3-Dioxolane-4,5-dicarboxamide, N-[[4-(aminoiminomethyl)phenyl]methyl]-N'-[(1R)-1-phenylethyl]-, (4R,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



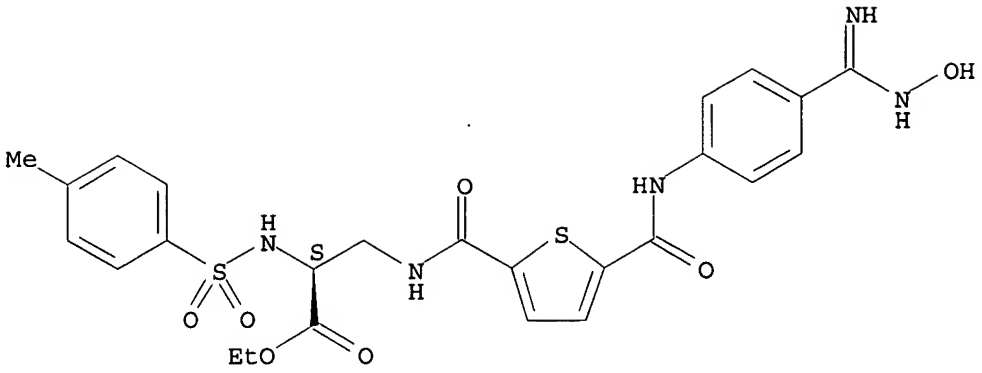
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN 1998:550423 CAPLUS
DN 129:175969
TI Preparation of .beta.-(arylcarbonylamino)alanines and analogs as fibrinogen receptor antagonist prodrugs
IN Egbertson, Melissa S.; Young, Steve D.; Hartman, George D.; Cook, Jacquelynn J.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9834935	A1	19980813	WO 1998-US1998	19980202
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9861413	A1	19980826	AU 1998-61413	19980202
	AU 747293	B2	20020516		
	EP 1023295	A1	20000802	EP 1998-906092	19980202
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	JP 2001512439	T2	20010821	JP 1998-534824	19980202
	US 5981584	A	19991109	US 1998-23650	19980203
PRAI	US 1997-36901P	P	19970206		
	GB 1997-7489	A	19970414		
	WO 1998-US1998	W	19980202		

OS MARPAT 129:175969
AB H2NC(:NOH)Z1Z2Z3CONHCH2CR2R3CO2R4 [I; R2,R3 = H, OH, CO2H, (un)substituted amino, etc.; R4 = H, alkyl, aryl, etc.; Z1 = (un)substituted phenylene; Z2 = (CH2)mZ(CH2)p; Z = bond, O, CO, NH, CONH, etc.; Z3 = heterocyclylene, (hetero)arylene, etc.; m,p = 0-6] were prepd. as fibrinogen receptor antagonist prodrugs (no data). Thus, 4-(NC)C6H4NO2 was etherified by 4-(HO)C6H4CO2H and the product amidated by (R)-H2NCH2CH(CO2Et)NHSO2C6H4Me-4 to give, after oximation, (R)-I (R2 = H, R3 = NHSO2C6H4Me-4, R4 = Et, Z1 = Z3 = 1,4-phenylene, Z2 = O).
IT **211487-95-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of .beta.-(arylcarbonylamino)alanines and analogs as fibrinogen receptor antagonist prodrugs)
RN 211487-95-5 CAPLUS
CN L-Alanine, 3-[[[5-[[[4-[(hydroxyamino)iminomethyl]phenyl]amino]carbonyl]-2-thienyl]carbonyl]amino]-N-[(4-methylphenyl)sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

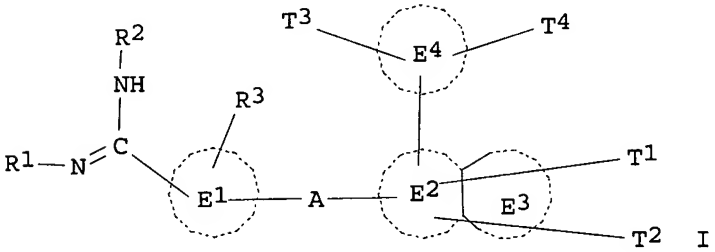


RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 1999:529128 CAPLUS
DN 131:184864
TI Preparation of amidinophenylcarbamoylbiphenyl derivatives and heterocyclic analogs thereof as inhibitors of blood coagulation factor VIIa
IN Senokuchi, Kazuhiko; Ogawa, Koji
PA Ono Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 665 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9941231	A1	19990819	WO 1999-JP622	19990212
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9923006	A1	19990830	AU 1999-23006	19990212
	EP 1078917	A1	20010228	EP 1999-902896	19990212
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	ZA 9901273	A	19990825	ZA 1999-1273	19990217
	US 6358960	B1	20020319	US 2000-601998	20000811
PRAI	JP 1998-76815	A	19980217		
	WO 1999-JP622	W	19990212		

OS MARPAT 131:184864
GI



I

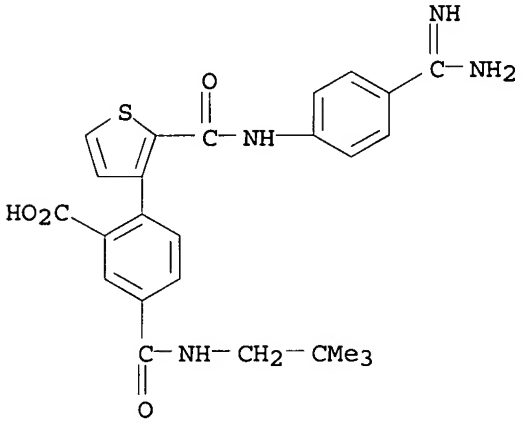
AB The title compds. I [T1 = (R5)q; T2 = (R7)n; T3 = (R6)m; T4 = (R4)p; R1, R2 = H, alkoxycarbonyl, etc.; a proviso is given; R3 = H, alkyl, etc.; ring E1 = unsatd. heterocyclic ring, etc.; ring E2 = unsatd. heterocyclic ring, etc.; ring E3 = unsatd. or satd. heterocyclic ring, etc.; ring E3 may be omitted; ring E4 = unsatd. heterocyclic ring, etc.; R4, R5 = CO2R8, etc.; R8 = H, alkyl, etc.; p, q = 0, or 1, 2; p + q = 1 or 2; R6, R7 = H, alkyl, etc.; m = 1 - 3; n = 1 - 3] are prepd. I are useful as preventives and/or remedies for various vascular lesions assocg. accelerated coagulation activity, for example, universal intravascular coagulation syndrome, coronary thrombosis, brain infarction, brain embolism, transient cerebral ischemic attack, diseases assocg. cerebral vascular disorders, deep vein thrombosis, peripheral embolism, thrombus formation following artificial blood vessel operation or artificial valve replacement, diseases assocg. postoperative thrombus formation, reobstruction and reconstriction following coronary artery bypass, reobstruction and

reconstriction following PTCA or PTCR, thrombus formation during extracorporeal circulation and glomerulonephritis. Formulations contg. a compd. of this invention are given. In an in vitro test, 2-[2-(4-amidinophenylcarbamoyl)-6-methoxy-3-pyridyl]-5-[(1(S)-hydroxymethyl-2,2-dimethylpropyl)carbamoyl]benzoic acid methanesulfonic acid salt showed IC50 of 0.013 .mu.M against factor VIIa.

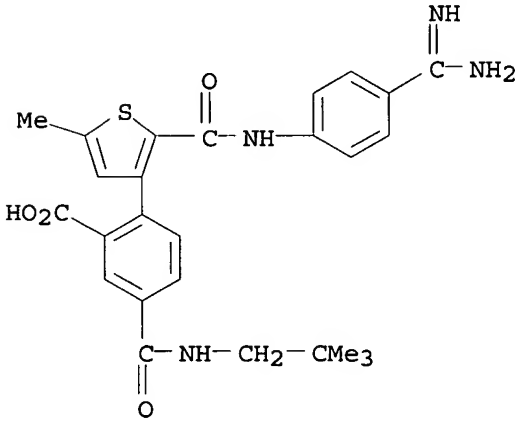
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d hitstr 4

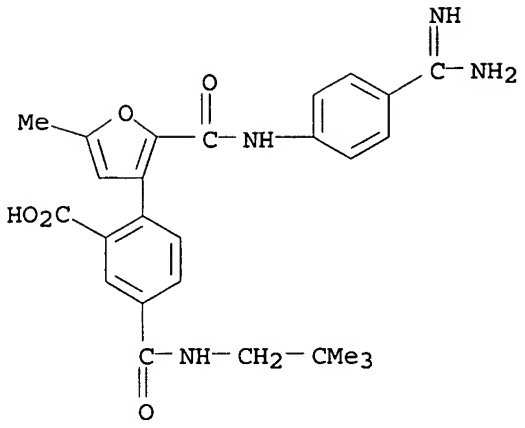
L11 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2003 ACS
IT **239459-97-3P 239460-01-6P 239460-05-0P**
239460-43-6P 239461-53-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and therapeutic effect of amidinophenylcarbamoylbiphenyl derivs. and heterocyclic analogs thereof)
RN 239459-97-3 CAPLUS
CN Benzoic acid, 2-[2-[[[4-(aminoiminomethyl)phenyl]amino]carbonyl]-3-thienyl]-5-[[(2,2-dimethylpropyl)amino]carbonyl]- (9CI) (CA INDEX NAME)



RN 239460-01-6 CAPLUS
CN Benzoic acid, 2-[2-[[[4-(aminoiminomethyl)phenyl]amino]carbonyl]-5-methyl-3-thienyl]-5-[[(2,2-dimethylpropyl)amino]carbonyl]- (9CI) (CA INDEX NAME)

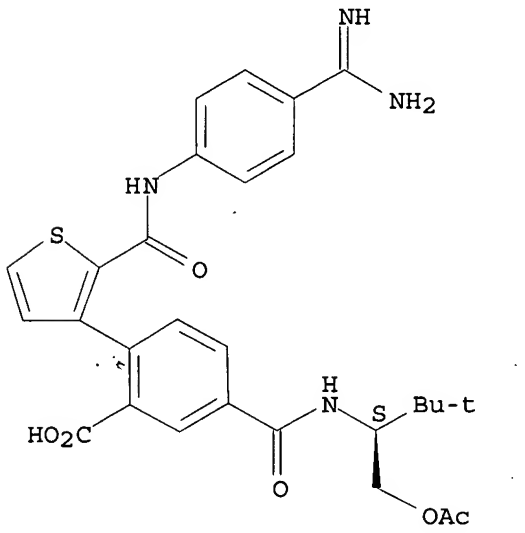


RN 239460-05-0 CAPLUS
CN Benzoic acid, 2-[2-[[[4-(aminoiminomethyl)phenyl]amino]carbonyl]-5-methyl-3-furanyl]-5-[[(2,2-dimethylpropyl)amino]carbonyl]- (9CI) (CA INDEX NAME)



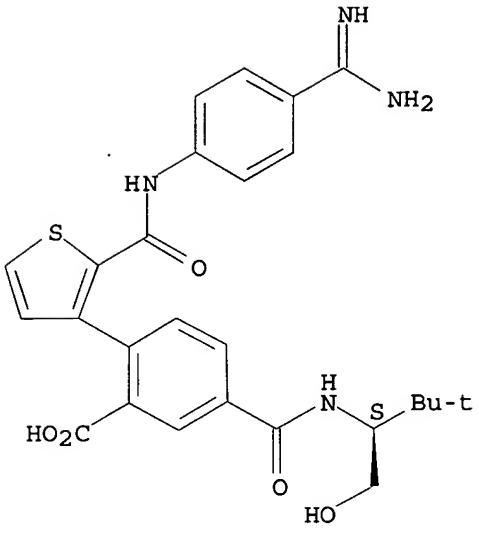
RN 239460-43-6 CAPLUS
CN Benzoic acid, 5-[[[(1S)-1-[(acetyloxy)methyl]-2,2-dimethylpropyl]amino]carbonyl]-2-[2-[[[4-(aminoiminomethyl)phenyl]amino]carbonyl]-3-thienyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 239461-53-1 CAPLUS
CN Benzoic acid, 2-[2-[[[4-(aminoiminomethyl)phenyl]amino]carbonyl]-3-thienyl]-5-[[[(1S)-1-(hydroxymethyl)-2,2-dimethylpropyl]amino]carbonyl]- (9CI) (CA INDEX NAME)

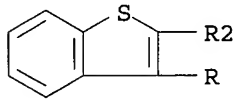
Absolute stereochemistry.

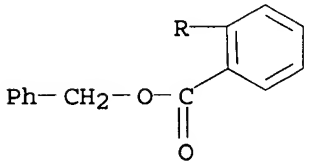


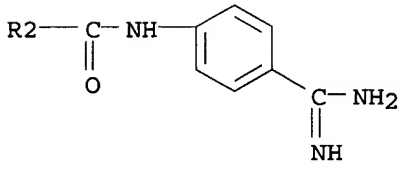
IT **239452-21-2P 239457-15-9P 239457-16-0P**
239458-70-9P 239458-77-6P 239458-79-8P
239458-81-2P 239459-02-0P 239459-85-9P
239459-86-0P 239459-98-4P 239460-02-7P
239460-06-1P 239460-44-7P 239461-54-2P
239463-51-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amidinophenylcarbamoylbiphenyl derivs. and heterocyclic analogs thereof as inhibitors of blood coagulation factor VIIa)

RN 239452-21-2 CAPLUS

CN Benzoic acid, 2-[2-[[[4-(aminoiminomethyl)phenyl]amino]carbonyl]benzo[b]thien-3-yl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

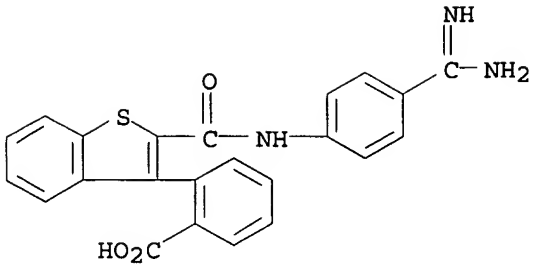






RN 239457-15-9 CAPLUS

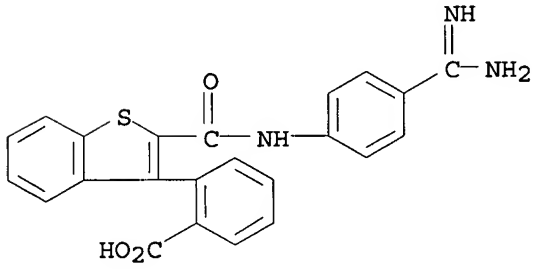
CN Benzoic acid, 2-[2-[[[4-(aminoiminomethyl)phenyl]amino]carbonyl]benzo[b]thien-3-yl]- (9CI) (CA INDEX NAME)



RN 239457-16-0 CAPLUS
CN Benzoic acid, 2-[2-[[[4-(aminoiminomethyl)phenyl]amino]carbonyl]benzo[b]th
ien-3-yl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

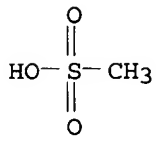
CM 1

CRN 239457-15-9
CMF C23 H17 N3 O3 S

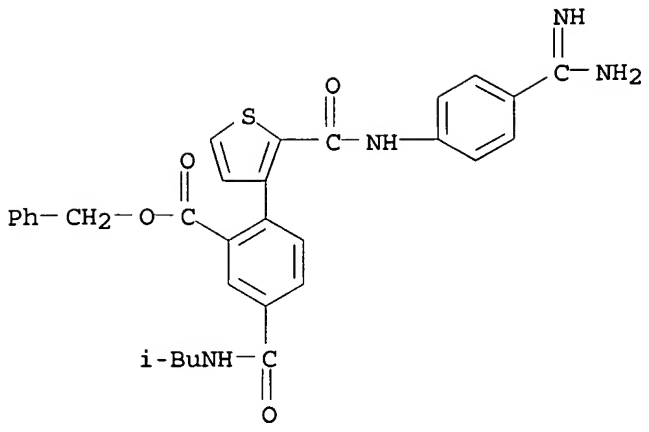


CM 2

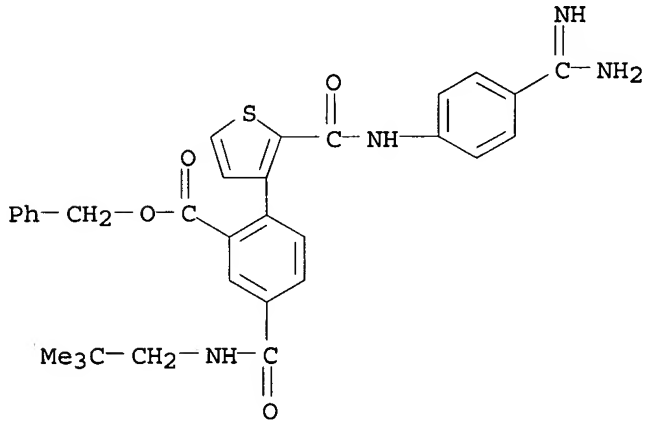
CRN 75-75-2
CMF C H4 O3 S



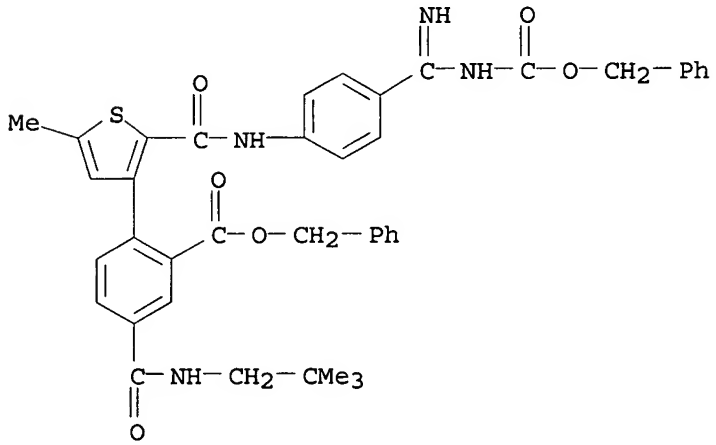
RN 239458-70-9 CAPLUS
CN Benzoic acid, 2-[2-[[[4-(aminoiminomethyl)phenyl]amino]carbonyl]-3-
thienyl]-5-[[(2-methylpropyl)amino]carbonyl]-, phenylmethyl ester (9CI)
(CA INDEX NAME)



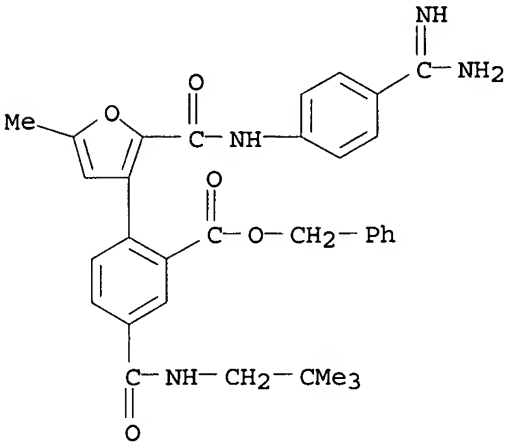
RN 239458-77-6 CAPLUS
CN Benzoic acid, 2-[2-[[[4-(aminoiminomethyl)phenyl]amino]carbonyl]-3-thienyl]-5-[[(2,2-dimethylpropyl)amino]carbonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 239458-79-8 CAPLUS
CN Benzoic acid, 5-[[(2,2-dimethylpropyl)amino]carbonyl]-2-[2-[[[4-[imino[[(phenylmethoxy)carbonyl]amino]methyl]phenyl]amino]carbonyl]-5-methyl-3-thienyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

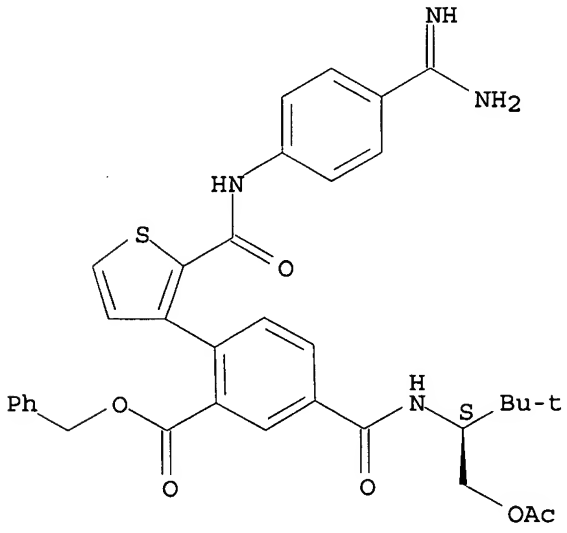


RN 239458-81-2 CAPLUS
CN Benzoic acid, 2-[2-[[[4-(aminoiminomethyl)phenyl]amino]carbonyl]-5-methyl-3-furanyl]-5-[[(2,2-dimethylpropyl)amino]carbonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

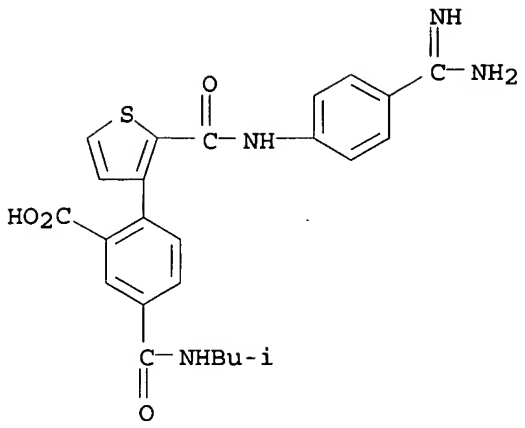


RN 239459-02-0 CAPLUS
CN Benzoic acid, 5-[[[(1S)-1-[(acetyloxy)methyl]-2,2-dimethylpropyl]amino]carbonyl]-2-[2-[[[4-(aminoiminomethyl)phenyl]amino]carbonyl]-3-thienyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



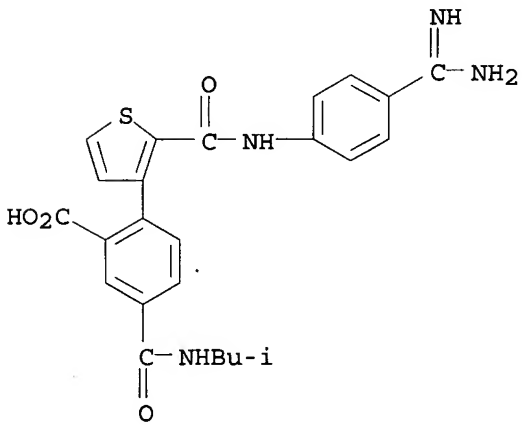
RN 239459-85-9 CAPLUS
CN Benzoic acid, 2-[2-[[[4-(aminoiminomethyl)phenyl]amino]carbonyl]-3-thienyl]-5-[[(2-methylpropyl)amino]carbonyl]- (9CI) (CA INDEX NAME)



RN 239459-86-0 CAPLUS
CN Benzoic acid, 2-[2-[[[4-(aminoiminomethyl)phenyl]amino]carbonyl]-3-thienyl]-5-[[(2-methylpropyl)amino]carbonyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

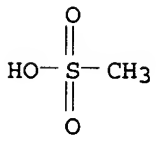
CM 1

CRN 239459-85-9
CMF C24 H24 N4 O4 S



CM 2

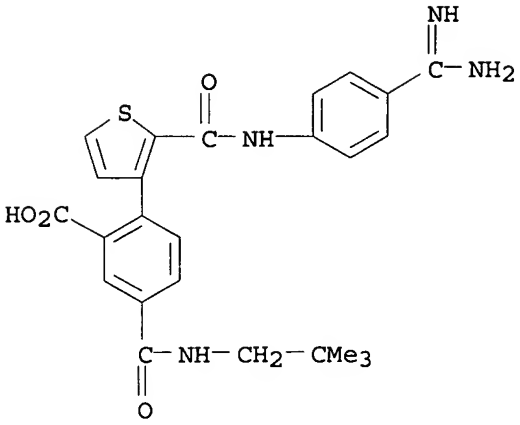
CRN 75-75-2
CMF C H4 O3 S



RN 239459-98-4 CAPLUS
CN Benzoic acid, 2-[2-[[[4-(aminoiminomethyl)phenyl]amino]carbonyl]-3-thienyl]-5-[[(2,2-dimethylpropyl)amino]carbonyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

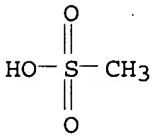
CM 1

CRN 239459-97-3
CMF C25 H26 N4 O4 S



CM 2

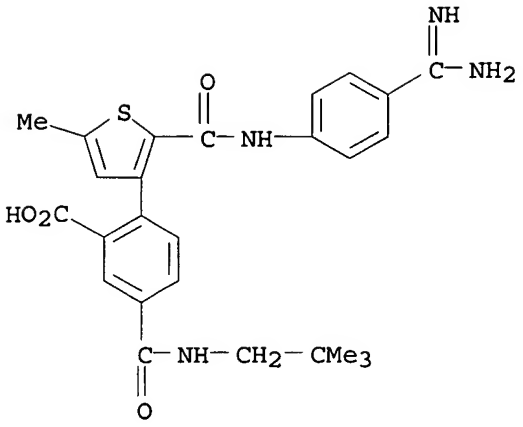
CRN 75-75-2
CMF C H4 O3 S



RN 239460-02-7 CAPLUS
CN Benzoic acid, 2-[2-[[[4-(aminoiminomethyl)phenyl]amino]carbonyl]-5-methyl-3-thienyl]-5-[[(2,2-dimethylpropyl)amino]carbonyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 239460-01-6
CMF C26 H28 N4 O4 S



CM 2

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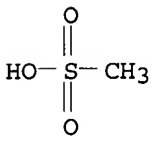
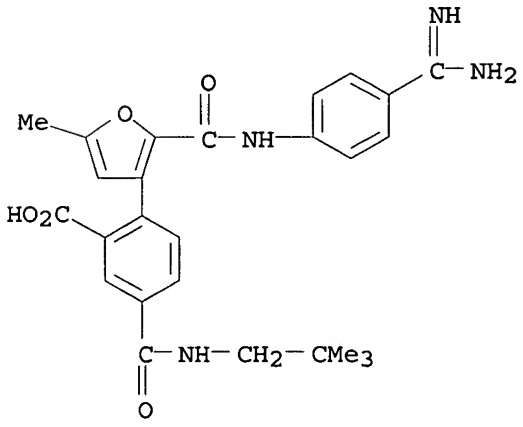
CMF C H4 O3 S



RN 239460-06-1 CAPLUS
CN Benzoic acid, 2-[2-[[[4-(aminoiminomethyl)phenyl]amino]carbonyl]-5-methyl-3-furanyl]-5-[[(2,2-dimethylpropyl)amino]carbonyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

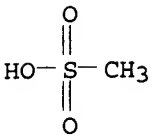
CRN 239460-05-0
CMF C26 H28 N4 O5



CM 2

CRN 75-75-2

CMF C H4 O3 S

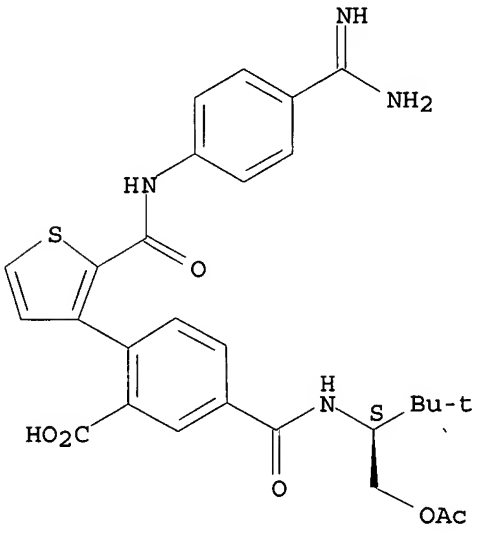


RN 239460-44-7 CAPLUS
CN Benzoic acid, 5-[[[(1S)-1-[(acetyloxy)methyl]-2,2-dimethylpropyl]amino]carbonyl]-2-[2-[[[4-(aminoiminomethyl)phenyl]amino]carbonyl]-3-thienyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

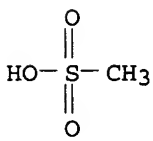
CRN 239460-43-6
CMF C28 H30 N4 O6 S

Absolute stereochemistry.



CM 2

CRN 75-75-2
CMF C H4 O3 S

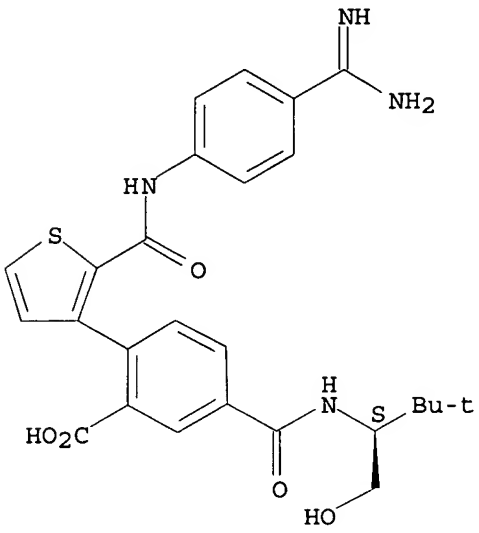


RN 239461-54-2 CAPLUS
CN Benzoic acid, 2-[2-[[[4-(aminoiminomethyl)phenyl]amino]carbonyl]-3-thienyl]-5-[[[(1S)-1-(hydroxymethyl)-2,2-dimethylpropyl]amino]carbonyl]-, monomethanesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 239461-53-1
CMF C26 H28 N4 O5 S

Absolute stereochemistry.



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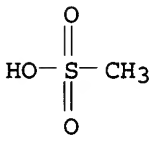
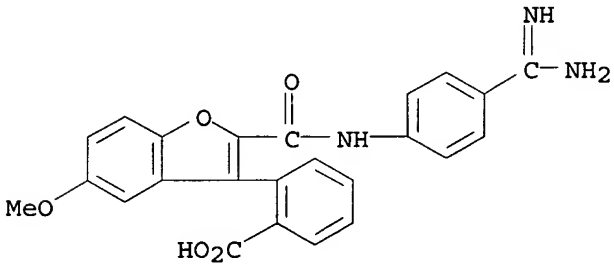


RN 239463-51-5 CAPLUS
CN Benzoic acid, 2-[2-[[[4-(aminoiminomethyl)phenyl]amino]carbonyl]-5-methoxy-3-benzofuranyl]- (9CI) (CA INDEX NAME)



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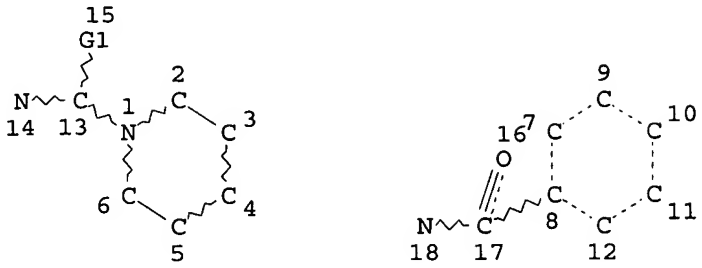

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DN   136:355487
TI   Preparation of meta-benzamidine derivatives of amino acids or dipeptides
     as serine protease inhibitors
IN   Liebeschuetz, John Walter; Wylie, William Alexander; Waszkowycz, Bohdan;
     Murray, Christopher William; Rimmer, Andrew David; Welsh, Pauline Mary;
     Jones, Stuart Donald; Roscoe, Jonathan Michael Ernest; Young, Stephen
     Clinton; Morgan, Phillip John
PA   UK
SO   U.S. Pat. Appl. Publ., 35 pp., Cont.-in-part of U.S. Ser. No. 485,678.
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DT   Patent
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FAN.CNT 13
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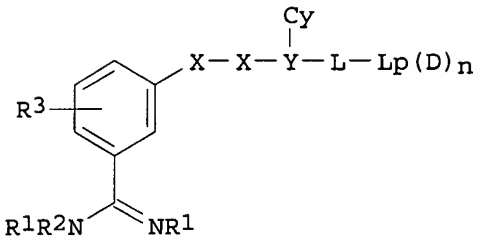

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AB Title compds. I [R1, R2 = H, OH, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, acyloxymethoxycarbonyl or alkylamino optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl, cycloalkyl; R3 = R1, R2, amino, halo, cyano, nitro, thiol, alkylthio, alkylsulfonyl, alkylsulfenyl, alkylsulfonamido, alkylaminosulfonyl, haloalkoxy, haloalkyl; X = C, N, O, S, CO, CR1, C(R1)2, NR1 with at least one X being C, CO, CR1 or C(R1)2, with the proviso that if the benzamidine group is unsubstituted and the X-X group is -CH2C(R1)2-, then R1 = H or attached to the alkylene carbon atom by a heteroatom; L = org. linker contg. 1-5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group; Y = N, CR1; YL = cyclic group; Cy = (un)satd., (poly)cyclic, (hetero)cyclic group optionally substituted by groups R3 or Ph optionally substituted by R3; Lp = lipophilic alkyl, heterocyclic, alkenyl, alkaryl, (poly)cycloalkyl, cycloalkenyl, aryl, aralkyl, haloalkyl, or a combination of two or more such groups optionally substituted by oxa, oxo, aza, thio, halo, amino, hydroxy or by R3; D = H bond donor group; n = 0-2], or corresponding compds. in which the (un)substituted amidino group R1R2NC(:NR1) is replaced with an (un)substituted aminomethyl group, or their physiol. tolerable salts were prepd. as serine protease inhibitors useful as antithrombotic agents. 3-Amidino- and 3-(aminomethyl)benzoyl-D-phenylglycine 4-aminomethylcyclohexylmethylamide are among 190 compds. synthesized.

L7 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2003 ACS
AN 1999:795787 CAPLUS
DN 132:35700
TI Preparation of benzamidine derivatives as activated blood coagulation factor X inhibitors
IN Nakagawa, Tadakiyo; Sagi, Kazuyuki; Yoshida, Kaoru; Fukuda, Yumiko; Shoji, Masataka; Takehana, Shunji; Kayahara, Takashi; Takahara, Akira
PA Ajinomoto Co., Inc., Japan
SO PCT Int. Appl., 143 pp.
CODEN: PIXXD2
DT **Patent**
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9964392	A1	19991216	WO 1999-JP3055	19990608 <--

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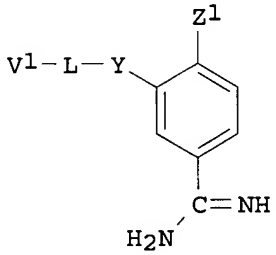
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2334476	AA	19991216	CA 1999-2334476	19990608	<--
AU 9940604	A1	19991230	AU 1999-40604	19990608	<--
EP 1086946	A1	20010328	EP 1999-923959	19990608	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI					
US 2001056123	A1	20011227	US 2000-731729	20001208	<--
US 6410538	B2	20020625			
US 2002107290	A1	20020808	US 2002-73985	20020214	<--
PRAI JP 1998-159627	A	19980608			
JP 1998-159628	A	19980608			
WO 1999-JP3055	W	19990608			
US 2000-731729	A1	20001208			

OS MARPAT 132:35700

GI



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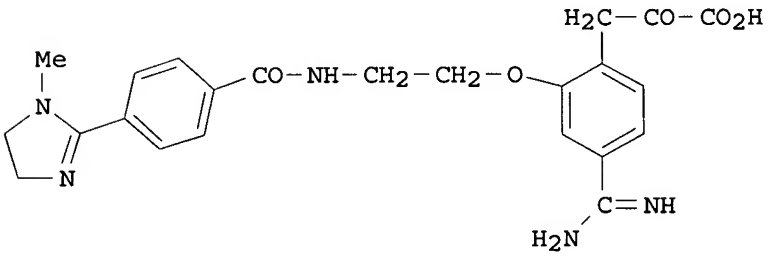


II

AB The title compds. I [L is CH2CH2, etc.; Z1 is CH:CHCOR2, etc.; R2 is OH, etc.; Y is CH:CH, etc.; V1 is, for example, H, (un)substituted benzoyl, etc.; extensive details on V1 are given] are prepd. I are useful as antithrombotics. In an in vitro test for inhibiting activity against activated blood coagulation factor X, the title compd. II.2CF3CO2H showed pIC50 of 8.1.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

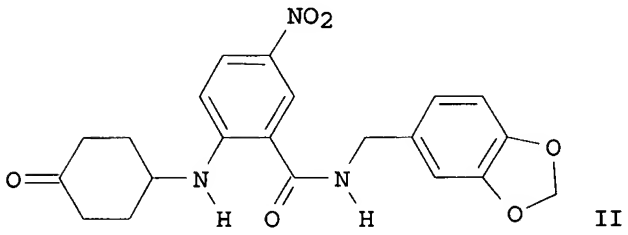
L7 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2003 ACS
AN 1999:691067 CAPLUS
DN 131:310451
TI Preparation of anthranilamides as of cGMP-phosphodiesterase inhibitors
IN Oku, Teruo; Sawada, Kozo; Kuroda, Akio; Inoue, Takayuki; Kayakiri, Natsuko; Sawada, Yuki; Mizutani, Tsuyoshi
PA Fujisawa Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 192 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	WO 9954284	A1	19991028	WO 1999-JP2028	19990415 <--
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2328413	AA	19991028	CA 1999-2328413	19990415 <--
	AU 9931708	A1	19991108	AU 1999-31708	19990415 <--
	BR 9909781	A	20001219	BR 1999-9781	19990415 <--
	EP 1080069	A1	20010307	EP 1999-913686	19990415
	EP 1080069	B1	20030319		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	JP 2001508811	T2	20010703	JP 1999-552766	19990415
	US 6384080	B1	20020507	US 2001-509541	20010423 <--
	US 2002193614	A1	20021219	US 2002-50789	20020118 <--
PRAI	AU 1998-3085	A	19980420		
	AU 1998-5851	A	19980911		
	AU 1998-7781	A	19981218		
	WO 1999-JP2028	W	19990415		
	US 2001-509541	A1	20010423		

OS MARPAT 131:310451

GI



II

AB R4NHZ1CONHZR3 [I; R3 = H, OH, alkoxy, aryl, etc.; R4 = alkoxy, heterocyclyl, (alkyl)amino, etc.; Z = alkylene; Z1 = e-withdrawing group-substituted (halo)-1,2-phenylene] were prepd. Thus, 2-fluoro-5-nitrobenzoic acid was amidated by 1,3-benzodioxole-5-methylamine and the product aminated by 4-aminocyclohexanol to give, after oxidn., title compd. II. Data for biol. activity of I were given.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2003 ACS

AN 1999:626174 CAPLUS

DN 131:243595

TI Preparation of piperidinyl and N-amidinopiperidinyl amino acid derivatives for inhibition of Factor Xa

IN Klein, Scott I.; Guertin, Kevin R.

PA Rhone-Poulenc Rorer Pharmaceuticals Inc., USA

SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2

DT **Patent**

LA English

FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 9948870 A1 19990930 WO 1999-US6224 19990322 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
CA 2325471 AA 19990930 CA 1999-2325471 19990322 <--
AU 9931094 A1 19991018 AU 1999-31094 19990322 <--
EP 1080075 A1 20010307 EP 1999-912798 19990322
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI
BR 9909086 A 20010904 BR 1999-9086 19990322
JP 2002507600 T2 20020312 JP 2000-537853 19990322
US 2002016339 A1 20020207 US 2001-922906 20010806 <--
PRAI US 1998-79002P A2 19980323
US 1999-273618 A3 19990322
WO 1999-US6224 W 19990322
OS MARPAT 131:243595
AB Compds. R1R2CHCHR3NR7COR4 [R1 = (CH2CH2)mZ3, (CH:CH)mZ3, or (CH2)nZ3, where m = 1 or 2; n = 0, 1, or 3; Z3 = substituted aryl, cycloalkyl, or cycloalkenyl, (un)substituted heteroaryl, heterocyclyl, heterocyclenyl,etc.; R2 = H, CO2R5, COR5, CONR52, CH2OR6, CH2SR6, where R5 = H, alkyl; R6 = H, (un)substituted alkyl, acyl, aroyl, heteroaroyl; R3 = H, (un)substituted alkyl, (CH2CH2)oZ2, (CH:CH)oZ2, (CH2)pZ2, where o = 1 or 2; p = 0, 1, or 3; Z2 = (un)substituted aryl, heteroaryl, cycloalkyl, cycloalkenyl, heterocyclyl, or heterocyclenyl; R4 = alkyl, alkenyl, alkynyl, (un)substituted cycloalkyl, heterocyclyl, aryl, heteroaryl, etc.; R7 = H, alkyl] were prepd. for inhibiting the activity of Factor Xa. Thus, N-(4-phenylbenzoyl)-2-(R)-(1,2,5,6-tetrahydro-3-pyridylmethyl)-3-(R)-.beta.-alanine Me ester was prepd. via alkylation/acylation of N-(tert-butoxycarbonyl)-3(R)-.beta.-alanine Me ester.
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

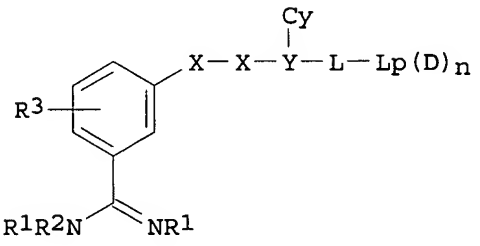
L7 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2003 ACS
AN 1999:184269 CAPLUS
DN 130:237884
TI Preparation of meta-benzamidine derivatives of amino acids or dipeptides as serine protease inhibitors
IN Liebeschuetz, John Walter; Wylie, William Alexander; Waszkowycz, Bohdan; Murray, Christopher William; Rimmer, Andrew David; Welsh, Pauline Mary; Jones, Stuart Donald; Roscoe, Jonathan Michael Ernest; Young, Stephen Clinton; Morgan, Phillip John
PA Proteus Molecular Design Ltd., UK
SO PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 13

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9911658	A1	19990311	WO 1998-GB2605	19980828 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9888757	A1	19990322	AU 1998-88757	19980828 <--

	EP 1009758	A1	20000621	EP 1998-940430	19980828 <--
	R: DE, FR, GB, IT				
	US 2002055522	A1	20020509	US 2001-988082	20011119 <--
PRAI	GB 1997-18392	A	19970829		
	GB 1998-3173	A	19980213		
	WO 1998-GB2605	W	19980828		
	GB 1999-13823	A	19990614		
	US 1999-142064P	P	19990702		
	US 2000-485678	A2	20000225		
	WO 2000-GB2291	A2	20000613		

OS MARPAT 130:237884

GI



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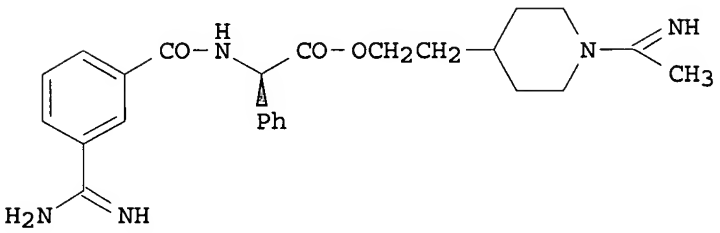


II

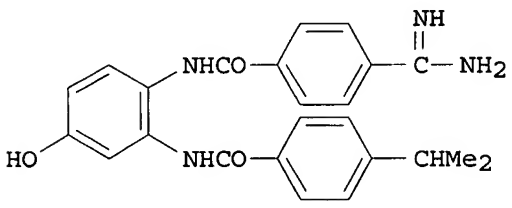
AB Title compds. I [R1, R2 = H, OH, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, acyloxymethoxycarbonyl or alkylamino optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl, cycloalkyl; R3 = R1, R2, amino, halo, cyano, nitro, thiol, alkylthio, alkylsulfonyl, alkylsulfenyl, alkylsulfonamido, alkylaminosulfonyl, haloalkoxy, haloalkyl; X = C, N, O, S, CO, CR1, C(R1)2, NR1 with at least one X being C, CO, CR1 or C(R1)2, with the proviso that if the benzamidine group is unsubstituted and the X-X group is -CH2C(R1)2-, then R1 = H or attached to the alkylene carbon atom by a heteroatom; L = org. linker contg. 1-5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group; Y = N, CR1; YL = cyclic group; Cy = (un)satd., (poly)cyclic, (hetero)cyclic group optionally substituted by groups R3 or Ph optionally substituted by R3; Lp = lipophilic alkyl, heterocyclic, alkenyl, alkaryl, (poly)cycloalkyl, cycloalkenyl, aryl, aralkyl, haloalkyl, or a combination of two or more such groups optionally substituted by oxa, oxo, aza, thio, halo, amino, hydroxy or by R3; D = H bond donor group; n = 0-2] and their physiol. tolerable salts were prepd. as serine protease inhibitors useful as antithrombotic agents. Synthesis methodol. for prepg. some I was provided, and common starting materials were Fmoc- or Boc-(D)-phenylglycine and m-amidinobenzoic acid. Descriptions of enzyme assays were given, but no enzyme inhibition data was provided for I. To measure the antithrombotic activity, a partial thromboplastin time test assay was done, and for example, m-amidinobenzoyl-D-phenylglycine ester II (prepn. not given, but 1H NMR characterization data provided), at 1.9 .mu.M concn., doubled the clotting

time.
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2003 ACS
AN 1999:42575 CAPLUS
DN 130:95393
TI Dibenzoylbenzenediamines as antithrombotic agents
IN Beight, Douglas Wade; Craft, Trelia Joyce; Franciskovich, Jeffry Bernard; Goodson, Theodore, Jr.; Hall, Steven Edward; Herron, David Kent; Klimkowski, Valentine Joseph; Masters, John Joseph; Mendel, David; Milot, Guy; Sawyer, Jason Scott; Shuman, Robert Theodore; Smith, Gerald Floyd; Tebbe, Anne Louise; Tinsley, Jennifer Marie; Weir, Leonard Crayton; Wikel, James Howard; Wiley, Michael Robert; Yee, Ying Kwong
PA Eli Lilly and Company, USA
SO PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI WO 9900127	A1	19990107	WO 1998-US13424	19980626	<--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9882706	A1	19990119	AU 1998-82706	19980626	<--
EP 1007037	A1	20000614	EP 1998-932926	19980626	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO					
JP 2002510313	T2	20020402	JP 1999-505827	19980626	
US 6417200	B1	20020709	US 2000-445970	20000509	<--
PRAI US 1997-50885P	P	19970626			
WO 1998-US13424	W	19980626			

OS MARPAT 130:95393
GI



I

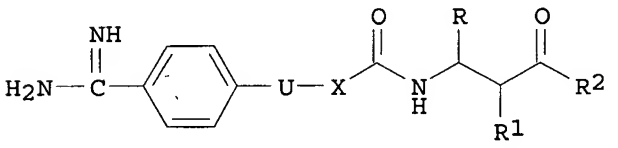
AB Title compds. were prepd. for use as inhibitors of factor Xa (no data). Thus, 4-amino-3-nitro phenol was silylated and acylated with 3-NCC6H4COCl to give 3-NCC6H4CONHC6H4(OSiMe2CMe3)NO2-4,2 which was reduced to the amine, acylated with 4-Me2CHC6H4COCl and desilylated to give 1-(3-NCC6H4CONH)C6H4(OH)(NHCOC6H4CHMe2-4)-4,2. This compd. was treated with NH2OH and then hydrogenated to give the diamide I.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2003 ACS

AN 1996:653632 CAPLUS
DN 125:329475
TI Aromatic compounds containing basic and acidic termini useful as fibrinogen receptor antagonists
IN Degrado, William F.; Xue, Chu-biao
PA The Dupont Merck Pharmaceutical Company, USA
SO U.S., 83 pp., Cont.-in-part of U.S. Ser. No. 174,552, abandoned.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5563158	A	19961008	US 1994-343159	19941122 <--
	WO 9518111	A1	19950706	WO 1994-US14244	19941221 <--
	W: AU, CA, CZ, FI, HU, JP, KR, NO, NZ, PL, SK				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9514000	A1	19950717	AU 1995-14000	19941221 <--
	US 5691329	A	19971125	US 1996-694043	19960808 <--
PRAI	US 1993-174552		19931228		
	US 1994-343159		19941122		
	WO 1994-US14244		19941221		

OS MARPAT 125:329475
GI



I

AB Title compds., such as I [U = OCH2, CH2O; X = m-C6H4, 3,5-isoxazolediyl; R = H, Me; R1 = (un)substituted amino; R2 = H, Me, Et] were prepd. for use as platelet aggregation inhibitors. Thus, L-H2NCH2CH(NH2)CO2Me was N-butanesulfonylated, treated with 3-ClC6H4COCl and 4-NCC6H4OH to give L-3-(4-NCC6H4OCH2)C6H4CONHCH2CH(NHSO2Bu)CO2Me which was subjected to aminolysis and ester hydrolysis to give L-3-[4-H2NC(:NH)C6H4OCH2]C6H4CONHCH2CH(NHSO2Bu)CO2H.CF3CO2H (II). II had an IC50 of <10 .mu.M in the fibrinogen binding assay for platelet aggregation.

L7 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2003 ACS
AN 1996:485770 CAPLUS
DN 125:142568
TI Preparation of novel N-imidoyl-[p-[(amidinonaphthylmethyl)amino]phenoxy]piperidine derivatives and analogs as blood platelet aggregation inhibitors
IN Hirayama, Fukushi; Koshio, Hiroyuki; Matsumoto, Yuzo; Kawasaki, Tomihisa; Kaku, Seiji; Yanagisawa, Isao
PA Yamanouchi Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 156 pp.
CODEN: PIXXD2
DT **Patent**
LA Japanese
FAN.CNT 1

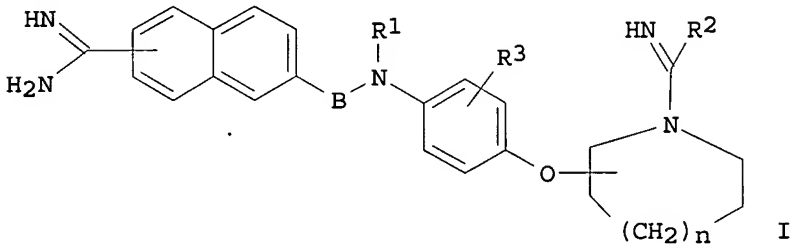
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9616940	A1	19960606	WO 1995-JP2458	19951201 <--
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,				

RO, RU, SD, SG, SI, SK, TJ, TM, TT, UA, US, UZ, VN
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2206532	AA	19960606	CA 1995-2206532	19951201	<--
AU 9539942	A1	19960619	AU 1995-39942	19951201	<--
AU 688628	B2	19980312			
EP 798295	A1	19971001	EP 1995-938625	19951201	<--
EP 798295	B1	20030226			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE					
CN 1167484	A	19971210	CN 1995-196546	19951201	<--
CN 1087736	B	20020717			
HU 77313	A2	19980330	HU 1997-2028	19951201	<--
JP 3004362	B2	20000131	JP 1996-518590	19951201	<--
RU 2154633	C2	20000820	RU 1997-108576	19951201	<--
PL 184824	B1	20021231	PL 1995-320486	19951201	
AT 233240	E	20030315	AT 1995-938625	19951201	
NO 9702482	A	19970801	NO 1997-2482	19970530	<--
US 5869501	A	19990209	US 1997-849391	19970530	<--
FI 9702326	A	19970602	FI 1997-2326	19970602	<--
PRAI JP 1994-299963	A	19941202			
JP 1995-105205	A	19950428			
JP 1995-198816	A	19950803			
WO 1995-JP2458	W	19951201			

OS MARPAT 125:142568

GI



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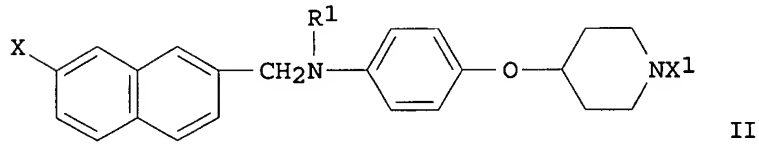

II

AB The title compds. [I; R1 = H or A-W-R4; wherein A = C(:X), COCO, SO2; X = O or S; W = a single bond or NR5; R4 = OH, lower alkoxy, (un)substituted lower alkyl, cycloalkyl, aryl, or heteroaryl; R5 = H, carbamoyl, lower alkoxycarbonyl, mono- or dialkylaminocarbonyl, lower alkylsulfonyl, mono- or dialkylaminothiocarbonyl, (un)substituted lower alkyl or alkanoyl; R2 = lower alkyl; R3 = H, halo, carboxy, NH2, cyano, NO2, OH, lower alkoxy, lower alkyl, lower alkoxycarbonyl; B = lower alkylene or carbonyl; n = 0 or 1], which have an antiplatelet aggregation effect on the basis of the effect of inhibiting activated blood coagulation factor X and are useful as antithrombotic agents, etc., are prepd. Thus, a cyanonaphthalene deriv. (II; R1 = Ac, X = cyano, X1 = Boc) (prepn. given, 128 mg) was dissolved in a mixt. of CH2Cl2 and EtOH , cooled to -20.degree., satd. with HCl(g), stirred at 5.degree. for 4 days, treated with a satd. methanolic NH3, and stirred at 5.degree. for 6 days to give an amidinonaphthalene deriv. II.2HCl (R1 = Ac, X = amidino, X1 = H) (92 mg), which (56 mg) was dissolved in EtOH, treated with 28 mg Et acetimidate

dihydrochloride and 36 mg Et3N, and stirred at room temp. for 2 days to give the title compd. II [R1 = Ac, X = amidino, X1 = C(:NH)Me]. II.2HCl [R1 = SO2NHCO2Et, X = amidino, X1 = C(:NH)Me] at 0.04 .mu.M in vitro prolonged twice the activated blood coagulation factor X-induced aggregation time of human serum as compared to 0.59 .mu.M for a ref. compd.

L7 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2003 ACS
AN 1995:890154 CAPLUS
DN 123:285548
TI Preparation of compounds containing basic and acidic termini useful as fibrinogen receptor antagonists
IN Degrado, William Frank; Xue, Chu-Biao
PA du Pont de Nemours, E. I., and Co., USA
SO PCT Int. Appl., 201 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9518111	A1	19950706	WO 1994-US14244	19941221 <--
	W: AU, CA, CZ, FI, HU, JP, KR, NO, NZ, PL, SK				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5563158	A	19961008	US 1994-343159	19941122 <--
	AU 9514000	A1	19950717	AU 1995-14000	19941221 <--
PRAI	US 1993-174552		19931228		
	US 1994-343159		19941122		
	WO 1994-US14244		19941221		

OS MARPAT 123:285548
AB The title compds. R1UVN(R6e)C(R7)(R8)C(R7a)(R9)R10 [R1 = (un)substituted amidinophenyl, (un)substituted amidinocyclohexyl, (un)substituted amidinoheterocyclyl, etc.; R6e = H, alkyl, alkenyl, cycloalkyl, aryl, etc.; R7, R7a = H, C1-4 alkyl; R8 = (un)substituted alkyl, (un)substituted alkenyl, (un)substituted alkynyl, (un)substituted cycloalkyl, (un)substituted aryl, etc.; R9 = H, (un)substituted alkenyl, (un)substituted alkynyl, etc.; R10 = tetrazolyl, (un)substituted CO2H, SO3H, PO3H, etc.; U = (un)substituted (CH2)3, (un)substituted CH2CH:CH, (un)substituted CH:CHCH2, etc.; V = heterocyclylcarbonyl or -sulfonyl bridging group], useful for the inhibition of platelet aggregation and/or for the treatment of thromboembolic disorders, are prepd. Thus, N-[3-(4-amidinophenyloxymethyl)benzoyl]-DL--3-aminobutyric acid trifluoroacetic acid salt was prepd. in 4 steps from 3-(chloromethyl)benzoyl chloride, and demonstrated a IC50 of <10 .mu.M in a thrombolytic assay based on human venous blood.

L7 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2003 ACS
AN 1995:812798 CAPLUS
DN 123:228897
TI Preparation of 1-amidinopiperdine and 4-amidinomorpholine blood platelet aggregation inhibitions
IN Ackermann, Jean; Banner, David; Gubernator, Klaus; Hilpert, Kurt; Schmid, Gerard
PA F. Hoffmann-La Roche AG, Switz.
SO Eur. Pat. Appl., 39 pp.
CODEN: EPXXDW
DT **Patent**
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 641779	A1	19950308	EP 1994-113488	19940830 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				

	TW 394760	B	20000621	TW 1994-83107736	19940823 <--
	CA 2130864	AA	19950308	CA 1994-2130864	19940825 <--
	ZA 9406671	A	19950307	ZA 1994-6671	19940831 <--
	IL 110834	A1	19980816	IL 1994-110834	19940901 <--
	AU 9472807	A1	19950323	AU 1994-72807	19940902 <--
	AU 684295	B2	19971211		
	HU 70616	A2	19951030	HU 1994-2527	19940902 <--
	US 5559232	A	19960924	US 1994-300821	19940902 <--
	JP 07112970	A2	19950502	JP 1994-234541	19940905 <--
	JP 2614984	B2	19970528		
	NO 9403294	A	19950308	NO 1994-3294	19940906 <--
	BR 9403448	A	19950516	BR 1994-3448	19940906 <--
	CN 1107839	A	19950906	CN 1994-109150	19940906 <--
	FI 9404100	A	19950308	FI 1994-4100	19940907 <--
	RU 2125991	C1	19990210	RU 1994-32284	19940907 <--
PRAI	CH 1993-2667	A	19930907		
	CH 1994-2150	A	19940705		

OS MARPAT 123:228897

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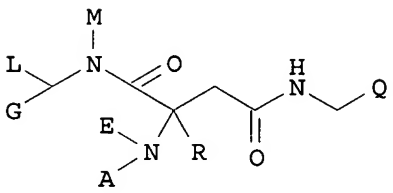


I

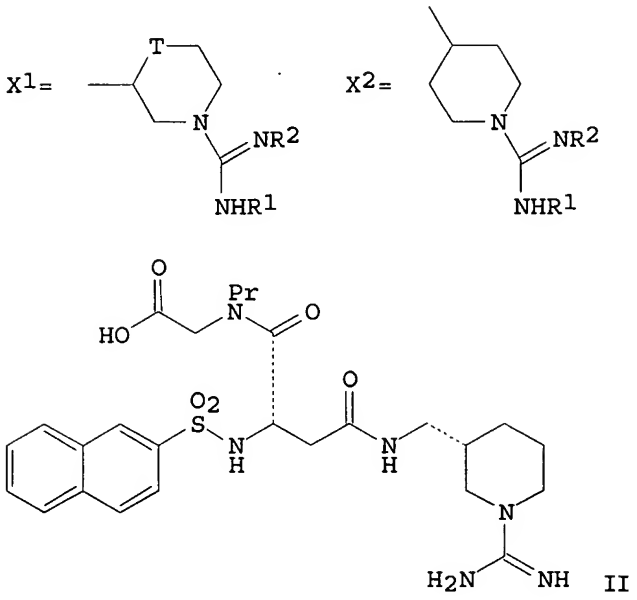
AB The title compds. [I; A = H, (un)substituted alkyl, (un)substituted carbonyl deriv., (un)substituted aminosulfonyl; E = H; G = H, alkyl, alkylcarboxy, alkanoyl, alkoxy, (un)substituted NH2, heteroaryl, etc.; L = H, alkyl, aryl, (un)substituted cycloalkyl, etc.; M = H, (un)substituted alkyl, alkenyl, aryl, heteroaryl, etc.; Q = (un)substituted 3- or 4-(1-amidinopiperidinyl), 2-(amidinomorpholinyl); R = H, alkyl] [e.g., Et [[(S)-3-[(S)-1-(aminoiminomethyl)piperidin-3-ylmethylcarbamoyl]-2-benzyloxycarbonylaminopropionyl]cyclopropylamino]acetate hydrochloride; Ki = 1.2 .mu.M thrombin; Ki = 70 .mu.M trypsin], useful for the treatment or prophylaxis of diseases which are caused by thrombin-induced platelet aggregation or the coagulation of fibrinogen in blood plasma, are prepd. and I-contg. formulations presented.

L7 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2003 ACS
AN 1994:483062 CAPLUS
DN 121:83062
TI N-Amidinopiperidinyl-(3/4)- or N-amidino-1,4-oxazinyl-(2)-substituted sulfonamides, process for their preparation, and use as thrombin inhibitors
IN Ackermann, Jean; Banner, David; Gubernator, Klaus; Hilpert, Kurt; Schmid, Gerard
PA Hoffmann-La Roche, F., und Co. A.-G., Switz.
SO Eur. Pat. Appl., 43 pp.
CODEN: EPXXDW
DT **Patent**
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 559046	A1	19930908	EP 1993-102767	19930222 <--
	EP 559046	B1	20010711		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

	CA 2089972	AA	19930907	CA 1993-2089972	19930219 <--
	AT 203013	E	20010715	AT 1993-102767	19930222
	ES 2161217	T3	20011201	ES 1993-102767	19930222
	US 5405854	A	19950411	US 1993-21919	19930224 <--
	ZA 9301403	A	19930906	ZA 1993-1403	19930226 <--
	AU 9333916	A1	19930909	AU 1993-33916	19930301 <--
	AU 665230	B2	19951221		
	IL 120727	A1	19980816	IL 1993-120727	19930301 <--
	HU 70156	A2	19950928	HU 1993-572	19930302 <--
	RO 112863	B3	19980130	RO 1993-294	19930303 <--
	BR 9300753	A	19930908	BR 1993-753	19930304 <--
	RU 2133739	C1	19990727	RU 1993-4666	19930304 <--
	NO 9300819	A	19930907	NO 1993-819	19930305 <--
	CN 1076690	A	19930929	CN 1993-101908	19930305 <--
	JP 06025195	A2	19940201	JP 1993-69080	19930305 <--
	JP 07080848	B4	19950830		
	PL 173030	B1	19980130	PL 1993-297960	19930305 <--
	CZ 286926	B6	20000816	CZ 1993-346	19930305 <--
	US 5578594	A	19961126	US 1994-361274	19941221 <--
	US 5677448	A	19971014	US 1996-689743	19960813 <--
	US 5763604	A	19980609	US 1997-869558	19970604 <--
	FI 9901361	A	19990614	FI 1999-1361	19990614 <--
PRAI	CH 1992-728	A	19920306		
	CH 1993-180	A	19930121		
	US 1993-21919	A3	19930224		
	IL 1993-104893	A3	19930301		
	FI 1993-990	A3	19930305		
	US 1994-361274	A3	19941221		
	US 1996-689743	A3	19960813		
OS	MARPAT 121:83062				
GI					



AB Title compds. ASO2N(Y)MCON(Q)CH2X [I; X = oxazinyl and piperidinyl groups X1 or X2; T = CH2 or O; R1, R2 = H, alkoxycarbonyl; Y = H and in some cases CH2CO2H or SO2A'; A, A' = (hetero)aryl, (cyclo)alkyl, heterocyclyl; Q = H, certain (un)substituted alkyl; M = CH(Z), CH(Z)CH2; Z = various

pendant groups, mostly contg. amide functions] were prepd. as drugs, primarily as inhibitors of thrombin-induced platelet aggregation and fibrinogen coagulation. For example, condensation of (S)-1-amidino-3-(aminomethyl)piperidine-2HCl with the corresponding acid by the BOP method gave (S)-[N-allyl-[3-[(S)-1-(aminoiminomethyl)piperidin-3-ylmethylcarbamoyl]-2-(2-naphthylsulfonylamino)propionyl]amino]acetic acid Et ester hydrochloride, which underwent hydrolysis by aq. NaOH and hydrogenation over Pd/C to give title compd. (S)-[[3-[(S)-1-(aminoiminomethyl)piperidin-3-ylmethylcarbamoyl]-2-(2-naphthylsulfonylamino)propionyl]propylamino]acetic acid (II). I showed high specificity for inhibition of thrombin over other serine proteases, with II having Ki = 0.22 and 4300 nM for thrombin and trypsin, resp. (ratio = 19,545). Approx. 200 I were prepd. in 73 synthetic examples.

L7 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2003 ACS
AN 1994:271189 CAPLUS
DN 120:271189
TI Aspartic acid derivatives, their preparation, and use as drugs
IN Klingler, Otmar; Zoller, Gerhard; Just, Melitta; Jablonka, Bernd
PA Cassella AG, Germany
SO Ger. Offen., 16 pp.
CODEN: GWXXBX
DT **Patent**
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	DE 4212304	A1	19931014	DE 1992-4212304	19920413	<--
	EP 565896	A2	19931020	EP 1993-104415	19930318	<--
	EP 565896	A3	19940112			
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE					
	EP 784058	A1	19970716	EP 1996-102404	19930318	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE					
	CZ 290280	B6	20020717	CZ 1993-494	19930324	
	US 5399570	A	19950321	US 1993-36923	19930325	<--
	AU 9336836	A1	19931014	AU 1993-36836	19930408	<--
	AU 659299	B2	19950511			
	CA 2093770	AA	19931014	CA 1993-2093770	19930408	<--
	ZA 9302535	A	19931104	ZA 1993-2535	19930408	<--
	IL 105355	A1	19980310	IL 1993-105355	19930409	<--
	SK 282125	B6	20011106	SK 1993-334	19930409	
	JP 07109256	A2	19950425	JP 1993-84946	19930412	<--
	HU 64016	A2	19931129	HU 1993-1071	19930413	<--
	HU 218206	B	20000628			
PRAI	DE 1992-4212304	A	19920413			
	EP 1993-104415	A3	19930318			

OS MARPAT 120:271189
AB Title derivs. H2NC(:NH)XNHCH(COR)CH2CO2H [I; X = NH(CH2)nC6H4CONMeCH2CO, NH(CH2)mZCONMeCH2CO (Z = cyclohexanediyl), NH(CH2)mC6H4OCH2CO, or NYAC6H4CO [Y = 2-9 CH2 groups bound to N to form a ring, A = (CH2)m, O, bond]; n = 1-4; m = 0-4; R = OH or NH2 or various derivs. of them] were prepd. (15 examples). I inhibit the binding of fibrinogen, fibronectin, and von Willebrand factor to integrin receptors, and are thus claimed as useful for inhibiting thrombocyte aggregation, metastasis of carcinoma cells, and the formation of osteoclasts on bone surface (no data). Thus, condensation of p-(4-piperidinylmethyl)benzoic acid with nitro-S-methylisothiourea gave 89% p-[4-(nitroamidinopiperidinyl)methyl]benzoic acid, which underwent DCC-mediated coupling with H2N-Asp(OCH2Ph)-Val-OCH2Ph (95%) followed by hydrogenolysis (94%) to give L,L-I [X = N[(CH2)2]2CHCH2C6H4CO-4, R = OH], i.e. p-[4-(N-amidinopiperidinyl)methyl]benzoyl-L-aspartyl-L-valine.

L7 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2003 ACS

AN 1993:517098 CAPLUS
DN 119:117098
TI Preparation of 2-pyrrolidinone-3-acetates and analogs as cell aggregation inhibitors
IN Austel, Volkhard; Eisert, Wolfgang; Himmelsbach, Frank; Linz, Guenter; Mueller, Thomas; Pieper, Helmut; Weisenberger, Johannes
PA Thomae, Dr. Karl, G.m.b.H., Germany
SO Eur. Pat. Appl., 73 pp.
CODEN: EPXXDW
DT **Patent**
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 528369	A2	19930224	EP 1992-113877	19920814 <--
	EP 528369	A3	19930421		
	EP 528369	B1	19991124		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	DE 4127404	A1	19930225	DE 1991-4127404	19910819 <--
	AT 186906	E	19991215	AT 1992-113877	19920814 <--
	CA 2076311	AA	19930220	CA 1992-2076311	19920818 <--
	NO 9203235	A	19930222	NO 1992-3235	19920818 <--
	AU 9221119	A1	19930225	AU 1992-21119	19920818 <--
	AU 654372	B2	19941103		
	JP 06025227	A2	19940201	JP 1992-219149	19920818 <--
	ZA 9206205	A	19940218	ZA 1992-6205	19920818 <--
	IL 102847	A1	19961114	IL 1992-102847	19920818 <--
	US 5455348	A	19951003	US 1993-173603	19931223 <--
PRAI	DE 1991-4127404		19910819		
	US 1992-929870		19920814		

OS MARPAT 119:117098
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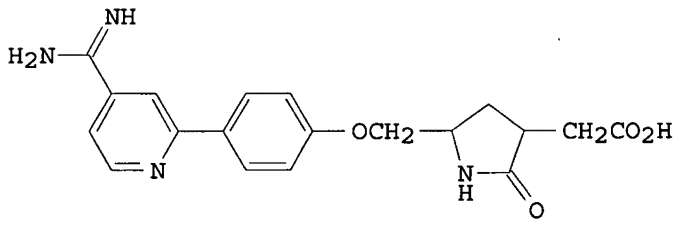

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AB EYAX1X2X3X4X5B [A = (substituted) bivalent (oxo)alkyleneimino; B = NH2, C(:NH)NH2, NHC(:NH)NH2, etc.; E = CO2H, alkoxycarbonyl, etc.; X1 = bond, alkylene; X2 = bond, O, NH, SO2NH, etc.; X3, X5 = (hetero)cycloalkylene, (hetero)arylene, etc.; X4 = bond, O, CH2, CO, NH, etc.; X3X4X5 = phenylene, (CH2)3-5, etc.; Y = alkylene, NHCH2, OCH2, etc.] were prepd. Thus, 4-(5-cyano-2-pyridyl)phenol (prepn. given) was condensed with (3S,5S)-3-[(tert-butyloxycarbonyl)methyl]-5-[(methanesulfonyloxy)methyl]-2-pyrrolidinone and the product converted in 2 steps to title compd. (3S,5S)-I which had EO50 of 0.06 .mu.M against collagen-induced platelet aggregation in vitro.

L7 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2003 ACS
AN 1992:612971 CAPLUS
DN 117:212971
TI Preparation of tripeptides as protease inhibitors
IN Abe, Yoshihito; Nagasawa, Takeshi; Kuroiwa, Katsumasa; Yaginuma, Katsuhiro
PA Nitto Boseki K. K., Japan
SO Jpn. Kokai Tokkyo Koho, 25 pp.

CODEN: JKXXAF
DT **Patent**
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	JP 04089498	A2	19920323	JP 1990-204492	19900801	<--
	JP 08013834	B4	19960214			
	US 5153176	A	19921006	US 1991-737708	19910730	<--
PRAI	JP 1990-204492		19900801			

OS MARPAT 117:212971
AB (D)-ANHCH[(CH2)4NHB]CO-Pro-X-H [I; A, B = (un)substituted arenesulfonyl, alkanesulfonyl, aroyl, acyl, cycloalkanesulfonyl, alkyloxycarbonyl, alkyl, aryl, or N-contg. heterocyclylsulfonyl, CHO, H, adamantyl, norbornyl; A = B .noteq. H; X = L-, D-, or DL-Arg], useful for treatment of trypsin-like serine protease-related diseases, e.g., inflammation, bleeding, allergy, nephritis, and ulcer, are prepd. Thus, esterification of Z-D-Lys(Tos)-OH with 2-mercapto-4,6-dimethylpyrimidine in the presence of DCC in EtOAc and coupling of the resulting active thiol ester with proline in the presence of Et3N gave Z-D-Lys(Tos)-Pro-OH which was coupled with H-Arg(Z)-OH .delta.-lactam.HCl (prepn. given) via formation of an active ester with ClCO2CHMe2 to give Z-D-Lys(Tos)-Pro-Arg(Z)-OH .delta.-lactam. Redn. of this with LiALH4 in THF at -30.degree. to Z-D-Lys(Tos)-Pro-Arg(Z)-H followed by hydrogenolysis over Pd black in 1N H2SO4-85% aq. MeOH gave H-D-Lys(Tos)-Pro-Arg-H.H2SO4. I.1/2H2SO4 (A = Me2CHO2C, B = Tos, X = Arg) in vitro showed IC50 (.times. 10-7) of 0.59, 4.4, 0.22, 0.37, 3.5, and 14 against plasmin, thrombin, trypsin, kallikrein, factor Xa, and urokinase.

L7 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2003 ACS
AN 1992:214908 CAPLUS
DN 116:214908
TI Preparation of (amidinoheterocyclylmethyl)amino acid sulfonamides and related compounds as thrombin inhibitors
IN Ackerman, Jean; Banner, David; Gubernator, Klaus; Hadvary, Paul; Hilpert, Kurt; Mueller, Klaus; Labler, Ludvik; Schmid, Gerard; Tschopp, Thomas; et al.
PA Hoffmann-La Roche, F., und Co. A.-G., Switz.
SO Eur. Pat. Appl., 41 pp.
CODEN: EPXXDW
DT **Patent**
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	EP 468231	A2	19920129	EP 1991-110928	19910702	<--
	EP 468231	A3	19920401			
	EP 468231	B1	19940921			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
	CA 2044636	AA	19920106	CA 1991-2044636	19910614	<--
	US 5260307	A	19931109	US 1991-719429	19910624	<--
	ZA 9105028	A	19920325	ZA 1991-5028	19910628	<--
	AU 9179490	A1	19920109	AU 1991-79490	19910701	<--
	AU 650458	B2	19940623			
	HU 58288	A2	19920228	HU 1991-2206	19910701	<--
	HU 217815	B	20000428			
	JP 04230363	A2	19920819	JP 1991-185774	19910701	<--
	JP 07030022	B4	19950405			
	IL 98690	A1	19960514	IL 1991-98690	19910701	<--
	IL 112712	A1	19960912	IL 1991-112712	19910701	<--
	ES 2061125	T3	19941201	ES 1991-110928	19910702	<--
	NO 9102626	A	19920106	NO 1991-2626	19910704	<--
	NO 177704	B	19950731			
	NO 177704	C	19951108			

	FI 9103282	A	19920106	FI 1991-3282	19910705 <--
	US 5393760	A	19950228	US 1993-77476	19930615 <--
	US 5532232	A	19960702	US 1994-343168	19941122 <--
	US 5595999	A	19970121	US 1995-473060	19950607 <--
	US 5583133	A	19961210	US 1995-511428	19950804 <--
	FI 9601629	A	19960412	FI 1996-1629	19960412 <--
	US 5763436	A	19980609	US 1996-715038	19960917 <--
PRAI	CH 1990-2250	A	19900705		
	CH 1991-1315	A	19910502		
	US 1991-719429	A3	19910624		
	IL 1991-98690	A3	19910701		
	FI 1991-3282	A	19910705		
	US 1993-77476	A3	19930615		
	US 1994-343168	A3	19941122		
	US 1995-473060	A3	19950607		

OS MARPAT 116:214908

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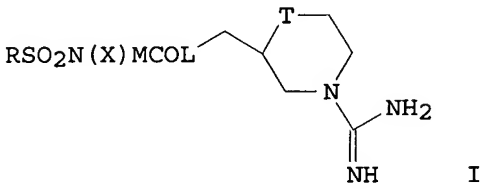

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AB Title compds. [I; R, R3 = (hetero)aryl, heterocyclyl; T = CH2, O; L = NH, O; N(X)M = N(SO2R3)CH2, (substituted) isoquinolinylene; X = H, CH2CO2H, alkoxycarbonylmethyl, alkyleneiminocarbonylmethyl, (alkylated) CH2CONH2; M = R1CH2CH, R1COCH2CH, PhCH2O2CNHCH2CH, etc.; R1 = (hetero)aryl, heterocyclyl, cycloalkyl], were prepd. Thus, tert-Bu R-4-hydroxymethyl-2,2-dimethyl-3-oxazolidinecarboxylate was successively tosylated, condensed with 2-indolinone using NaH in DMF, and treated with 2N HCl to give 1-[(R)-2-amino-3-hydroxypropyl]-2-indolinone. This was acylated with 2-naphthylsulfonyl chloride followed by Jones oxidn. to give N-(2-naphthylsulfonyl)-3-(2,3-dioxo-1-indolinyl)-D-alanine. This was converted to (R)-N-[(RS)-1-aminido-3-piperidinylmethyl]-.alpha.-(2-naphthylsulfonamido-2,3-dioxo-1-indolinepropionamide acetate. The latter inhibited thrombin with Ki = 8.55 nM and trypsin with Ki = 20,075.

L7 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2003 ACS
AN 1991:492947 CAPLUS
DN 115:92947
TI Preparation of N-amidobenzoyl-.beta.-alanines and analogs as fibrinogen antagonists and antitumor agents
IN Alig, Leo; Edenhofer, Albrecht; Mueller, Marcel; Trzeciak, Arnold; Weller, Thomas
PA Hoffmann-La Roche, F., und Co. A.-G., Switz.
SO Eur. Pat. Appl., 28 pp.
CODEN: EPXXDW
DT **Patent**
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 372486	A2	19900613	EP 1989-122396	19891205 <--
	EP 372486	A3	19910612		
	EP 372486	B1	19940601		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	US 5039805	A	19910813	US 1989-440949	19891124 <--

	CA 2004127	AA	19900608	CA 1989-2004127	19891129 <--
	ZA 8909210	A	19900829	ZA 1989-9210	19891201 <--
	IL 92518	A1	19941129	IL 1989-92518	19891201 <--
	HU 53068	A2	19900928	HU 1989-6350	19891204 <--
	HU 206192	B	19920928		
	AU 8945865	A1	19901101	AU 1989-45865	19891204 <--
	AU 648751	B2	19940505		
	AT 106389	E	19940615	AT 1989-122396	19891205 <--
	ES 2054995	T3	19940816	ES 1989-122396	19891205 <--
	DK 8906153	A	19900609	DK 1989-6153	19891206 <--
	DK 171888	B1	19970804		
	NO 8904919	A	19900611	NO 1989-4919	19891207 <--
	JP 02223543	A2	19900905	JP 1989-320391	19891208 <--
	JP 06010179	B4	19940209		
PRAI	CH 1988-4543		19881208		
	CH 1989-3703		19891011		
	EP 1989-122396		19891205		

OS MARPAT 115:92947

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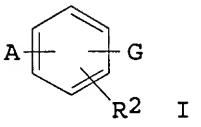


I .

AB The title compds. [I; A = R1CONH(CH2)i; G = (CH2)jCONHCHR1CH2CO2H; R1 = CHRa(CH2)nNHR6, T1C6H4CH2NHRc, TmC6H4(NH)pC(:NH)NH2, aminomethylcyclohexyl, etc.; Ra = H, NH2, alkoxycarbonylamino, NHCO2CH2Ph, NHCOCH2NYCH2CH2NHY; R6 = H, amidino, C(:NH)(CH2)hMe; Rc = H, amidino; R2 = H, me, OMe, NO2, halo, etc.; R3 = H, CONH2, CORf, CO2Rg; Rf= N-linked amino acid residue; Rg = H, alkyl; T = CH2, CH:CH, CHRdCH2; Rd = groups cited for Ra, NHBz, NHCOC6H4N3, arylsulfonylamino; Y = H, CO2CMe3, CO2CH2Ph; i, j, l, m, p = 0,1; k = 0-3; n = 1-6] were prepd. Thus, RCl [R = 4-[H2N(HN:)C]C6H4CO] was condensed with 3-(R4HN)C6H4CONHCH2CH2CO2R5 (II; R4 = H, R5 = CH2Ph) to give, after hydrogenolysis, II (R4 = R, R5 = H) which had IC50 of 10-4 .mu.M against fibrinogen binding to glycoprotein IIb/IIIa.

L7 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2003 ACS

AN 1981:192706 CAPLUS

DN 94:192706

TI Peptidyl-NG-carboxyargininealdehydes

IN Bajusz, Sandor; Szell, Erzesebet; Barabas, Eva; Bagdy, Daniel

PA Richter, Gedeon, Vegyeszeti Gyar Rt., Hung.

SO Ger. Offen., 37 pp.
CODEN: GWXXBX

DT **Patent**

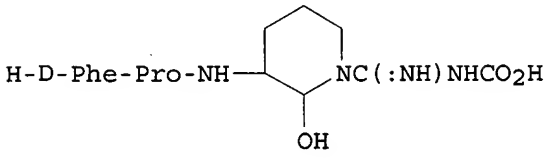
LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3000225	A1	19800724	DE 1980-3000225	19800104 <--
	DE 3000225	C2	19891019		
	HU 19372	O	19810128	HU 1979-GO1435	19790104 <--
	HU 177098	P	19810728		
	IL 58978	A1	19820930	IL 1979-58978	19791217 <--
	ZA 7906895	A	19801231	ZA 1979-6895	19791219 <--
	BE 880844	A1	19800624	BE 1979-9666	19791224 <--
	JP 55122749	A2	19800920	JP 1979-168478	19791226 <--
	JP 59051936	B4	19841217		

	AU 7954207	A1	19800710	AU 1979-54207	19791227 <--
	AU 533343	B2	19831117		
	FR 2445826	A1	19800801	FR 1979-31744	19791227 <--
	FR 2445826	B1	19841123		
	NO 7904327	A	19800707	NO 1979-4327	19791228 <--
	NO 151085	B	19841029		
	NO 151085	C	19850206		
	US 4316889	A	19820223	US 1979-108224	19791228 <--
	FI 8000008	A	19800705	FI 1980-8	19800102 <--
	FI 67539	B	19841231		
	FI 67539	C	19850410		
	SE 8000032	A	19800705	SE 1980-32	19800102 <--
	SE 448461	B	19870223		
	SE 448461	C	19870702		
	AT 8000012	A	19830115	AT 1980-12	19800102 <--
	AT 372076	B	19830825		
	DK 8000038	A	19800705	DK 1980-38	19800103 <--
	DK 149895	B	19861020		
	DK 149895	C	19870421		
	CH 643820	A	19840629	CH 1980-7	19800103 <--
	SU 1366062	A3	19880107	SU 1980-2861956	19800103 <--
	NL 8000040	A	19800708	NL 1980-40	19800104 <--
	NL 191537	B	19950501		
	NL 191537	C	19950904		
	ES 487464	A1	19801101	ES 1980-487464	19800104 <--
	CA 1133897	A1	19821019	CA 1980-343115	19800104 <--
PRAI	HU 1979-GO1435		19790104		

GI



III

AB R-X-Pro-NHCH(CHO)(CH2)3NHC(:NH)NHCO2H [I; R = H, Bz, Me3CO2C (BOC); X = D-Phe, D-allo-Ile, .beta.-phenyl-D-lactic acid residue] were prepd. as blood-clotting inhibitors. Thus, BOC-Arg-OH was treated with Z-Cl (Z = PhCH2O2C) to give 73.5% BOC-Arg(Z)-OH, which was cyclized by ClCO2CH2CHMe2 in THF to give 67% of the corresponding arginine lactam. The latter was BOC-deblocked by HCl and then coupled to Z-D-Phe-Pro-OH by ClCO2CH2CHMe2 to give 88% of the protected tripeptide lactam, which was reduced by LiAlH4 to give 73% of the corresponding tripeptide aldehyde. The latter was Z-deblocked by hydrogenolysis to give 96.4% I (R = H, X = D-Phe) (II). The cyclic form of II, cyclic carbinol III, was also claimed. Tabular data for the above biol. activity of I are given.

L7 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2003 ACS
AN 1974:108545 CAPLUS
DN 80:108545
TI [(Aminoalkylidene)amino]triiodobenzamide derivatives for x-ray contrast medium
IN Obendorf, Werner; Lindner, Irmgard; Schwarzinger, Ernst; Krieger, Josef
PA Lentia G.m.b.H., Chem. u. Pharm. Erzeugnisse-Industriebedarf
SO Ger. Offen., 35 pp.
CODEN: GWXXBX
DT **Patent**
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	DE 2235935	A1	19740207	DE 1972-2235935	19720721 <--
	DE 2235935	C3	19790726		
	DE 2235935	B2	19781130		
	FI 61872	B	19820630	FI 1973-2139	19730704 <--
	FI 61872	C	19821011		
	GB 1443062	A	19760721	GB 1973-33382	19730712 <--
	HU 166753	P	19750528	HU 1973-OE205	19730713 <--
	ZA 7304829	A	19740626	ZA 1973-4829	19730716 <--
	DD 107908	Z	19740820	DD 1973-172320	19730717 <--
	CA 1002522	A1	19761228	CA 1973-176658	19730717 <--
	FR 2193621	A1	19740222	FR 1973-26277	19730718 <--
	CH 590061	A	19770729	CH 1973-10592	19730719 <--
	CS 191903	P	19790731	CS 1973-5198	19730719 <--
	NL 7310136	A	19740123	NL 1973-10136	19730720 <--
	NL 163207	B	19800317		
	NL 163207	C	19800815		
	US 3890318	A	19750617	US 1973-381337	19730720 <--
	IT 991822	A	19750830	IT 1973-69187	19730720 <--
	PL 85383	P	19760430	PL 1973-164196	19730720 <--
	SU 514566	D	19760515	SU 1973-1948994	19730720 <--
	RO 62908	P	19780215	RO 1973-75545	19730720 <--
	SE 402101	B	19780619	SE 1973-10162	19730720 <--
	SE 402101	C	19780928		
	RO 63770	B1	19780915	RO 1973-83230	19730720 <--
	RO 64154	P	19790115	RO 1973-83226	19730720 <--
	JP 49055639	A2	19740530	JP 1973-80842	19730721 <--
	JP 55037548	B4	19800929		
	ES 417136	A1	19760316	ES 1973-417136	19730721 <--
	BE 806667	A1	19740429	BE 1973-137192	19731029 <--
	US 4025550	A	19770524	US 1975-562933	19750328 <--
PRAI	DE 1972-2235935		19720721		
	FR 1973-26277		19730718		
	US 1973-381337		19730720		

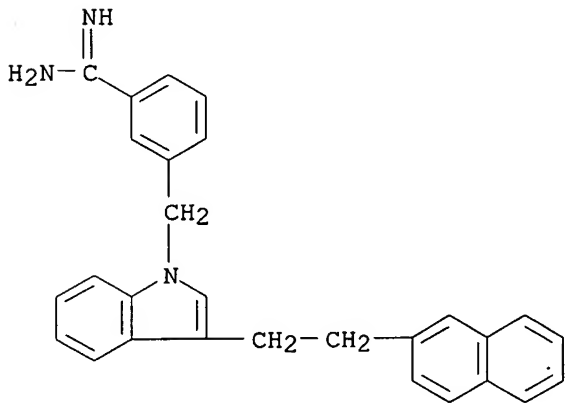
GI For diagram(s), see printed CA Issue.

AB Fifty-nine triiodobenzamides [I; R = H, Me, Et, Pr, CHMe2, CH2,Ch:CH2, (CH2)3OMe, Ph, or CH2Ph; R1 = Me, Et, CH2CH:CH2 or QCO2H with Q = CH2CHMe, CHMeCH2, (CH2)n, n = 1, 2, or 5; or NRR1 = morpholino; R2 = H, Me, Et, or (CH2)2CO2H; R3 = H, Me, or Et; R4 = Me, Et, or Ph; or NR3R4 = piperidino or morpholino; R5 = H, CO2H, or CONHMe], useful as x-ray contrast medium esp. for the cholecystog., were prepd. by reaction of II (X = Cl, Z = H) with POCl3 and R2CONR3R4 (III) and subsequently with RR1NH (IV) and in the case of the reaction with IV (R1 = QCO2Me) followed by sapon., by reaction of II (X = NRR1, Z = H) with POCl3 and III, or by reaction of II (X = NRR1, Z = COR2) with PCl5 and R3R4NH optionally followed by sapon.

AN 1999:529820 CAPLUS
DN 131:295103
TI Design and Structure-Activity Relationships of Potent and Selective Inhibitors of Blood Coagulation Factor Xa
AU Ewing, William R.; Becker, Michael R.; Manetta, Vincent E.; Davis, Roderick S.; Pauls, Henry W.; Mason, Helen; Choi-Sledeski, Yong Mi; Green, Daniel; Cha, Don; Spada, Alfred P.; Cheney, Daniel L.; Mason, Jonathan S.; Maignan, Sebastien; Guilloteau, Jean-Pierre; Brown, Karen; Colussi, Dennis; Bentley, Ross; Bostwick, Jeff; Kasiewski, Charles J.; Morgan, Suzanne R.; Leadley, Robert J.; Dunwiddie, Christopher T.; Perrone, Mark H.; Chu, Valeria
CS Departments of Cardiovascular Drug Discovery and New Leads Generation, Rhone-Poulenc Rorer, Collegeville, PA, 19426-0107, USA
SO Journal of Medicinal Chemistry (1999), 42(18), 3557-3571
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 131:295103
AB The discovery of a series of non-peptide factor Xa (FXa) inhibitors incorporating 3-(S)-amino-2-pyrrolidinone as a central template is described. After identifying compd. 4, improvements in in vitro potency involved modifications of the lipophilic group and optimizing the angle of presentation of the amidine group to the S1 pocket of FXa. These studies ultimately led to compd. RPR120844, a potent inhibitor of FXa (Ki = 7 nM) which shows selectivity for FXa over trypsin, thrombin, and several fibrinolytic serine proteinases. RPR120844 is an effective anticoagulant in both the rat model of FeCl2-induced carotid artery thrombosis and the rabbit model of jugular vein thrombus formation.
IT **247030-99-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(design and structure-activity relationships of potent and selective inhibitors of blood coagulation factor Xa in relation to antithrombotic activity)
RN 247030-99-5 CAPLUS
CN Benzenecarboximidamide, 3-[[3-[2-(2-naphthalenyl)ethyl]-1H-indol-1-yl]methyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

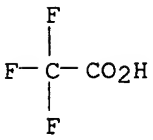
CM 1

CRN 247030-98-4
CMF C28 H25 N3



CM 2

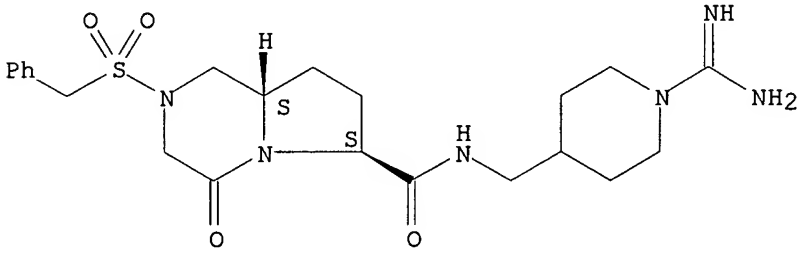
CRN 76-05-1
CMF C2 H F3 O2



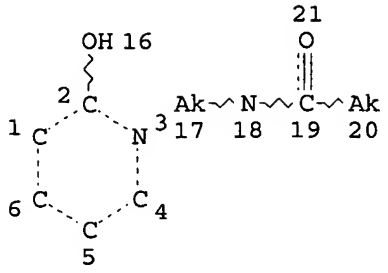
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

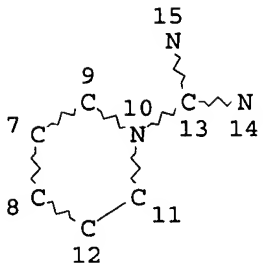
AN 2001:872229 CAPLUS
DN 136:210039
TI Novel bicyclic lactam inhibitors of thrombin: potency and selectivity optimization through P1 residues
AU Levesque, Sophie; St. Denis, Yves; Bachand, Benoit; Preville, Patrice; Leblond, Lorraine; Winocour, Peter D.; Edmunds, Jeremy J.; Rubin, J. R.; Siddiqui, M. Arshad
CS Shire BioChem Inc., Laval, QC, H7V 4A7, Can.
SO Bioorganic & Medicinal Chemistry Letters (2001), 11(24), 3161-3164
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB Peptidomimetic inhibitors of thrombin lacking the important Ser195-carbonyl interaction have been prepd. The binding energy lost after the removal of the activated carbonyl was recaptured through a series of modifications of the P1 residues of the bicyclic lactam inhibitors. Selected substituted compds. displayed useful pharmacol. profiles both in vitro and in vivo.
IT **401947-02-2P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of novel peptidomimetic bicyclic lactam inhibitors of thrombin and their potency and selectivity optimization through P1 residues)
RN 401947-02-2 CAPLUS
CN Pyrrolo[1,2-a]pyrazine-6-carboxamide, N-[[1-(aminoiminomethyl)-4-piperidinyl]methyl]octahydro-4-oxo-2-[(phenylmethyl)sulfonyl]-, (6S,8aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT





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FULL SCREEN SEARCH COMPLETED - 276 TO ITERATE

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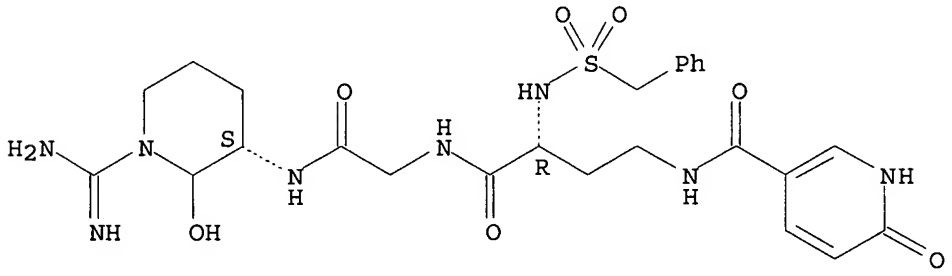
L6 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN 261367-55-9 REGISTRY
CN 3-Pyridinecarboxamide, N-[(3R)-4-[[2-[[(3S)-1-(aminoiminomethyl)-2-hydroxy-3-piperidinyl]amino]-2-oxoethyl]amino]-4-oxo-3-[[(phenylmethyl)sulfonyl]amino]butyl]-6-hydroxy- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C25 H34 N8 O7 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

AN 2000:9751 CAPLUS
DN 132:216542
TI Exploratory solid-phase synthesis of factor Xa inhibitors: discovery and application of P3-heterocyclic amides as novel types of non-basic arginine surrogates
AU Ho, Jonathan Z.; Levy, Odile E.; Gibson, Tony S.; Nguyen, Khanh; Semple, J. Edward
CS Department of Medicinal Chemistry, Corvas International, Inc., San Diego, CA, 92121, USA
SO Bioorganic & Medicinal Chemistry Letters (1999), 9(24), 3459-3464
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
GI

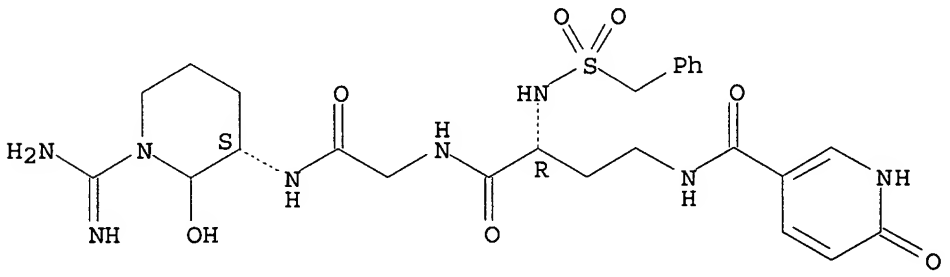
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A series of novel FXa inhibitors I (n = 0-2), II (R = 3-bromo-5-pyridinyl, 1-isoquinolinyl, 3-quinolinyl, 2-hydroxy-5-pyridinyl, 3-pyridinyl, 4-cinnolinyl, 2-quinolinyl, 2-hydroxy-3-quinoxalinyl, Ph, 2-pyridinyl) and III (R = 2-pyrazinyl, 2-methyl-5-pyrazinyl, 3-pyrazoyl, 3-bromo-5-pyridinyl, 1-isoquinolinyl, 3-quinolinyl) that feature heterocyclic carboxamides attached to a (D)-2,4-diaminobutyric acid side chain was discovered. These neutral amide derivs. serve as novel P3 D-arginine mimics. Pyrazine carboxamide scaffolds afforded the most potent FXa inhibitors [e.g., I (n = 1) IC50 = 4.6 nM]. The synthesis and biol. activity of I, II and III are reported.

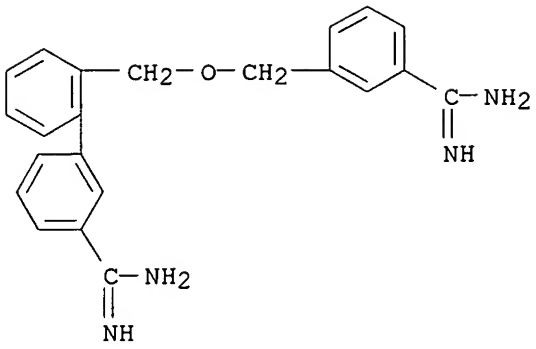
IT **261367-55-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(solid-phase synthesis and biol. activity of diaminobutyrate heterocyclic amides as factor Xa inhibitors)

RN 261367-55-9 CAPLUS
CN 3-Pyridinecarboxamide, N-[(3R)-4-[[2-[[(3S)-1-(aminoiminomethyl)-2-hydroxy-3-piperidinyl]amino]-2-oxoethyl]amino]-4-oxo-3-[[(phenylmethyl)sulfonyl]amino]butyl]-6-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT



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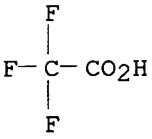
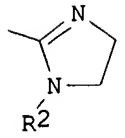
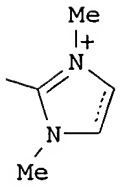
CRN 76-05-1
CMF C2 H F3 O2

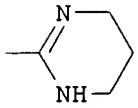


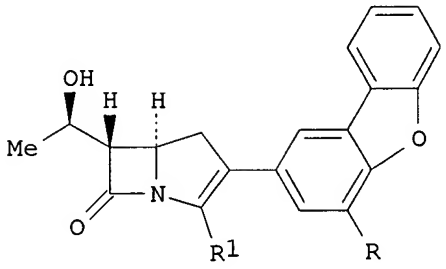
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:716677 CAPLUS
DN 132:64081
TI The synthesis and anti-MRSA activity of amidinium-substituted 2-dibenzofuranylcarbapenems
AU Laub, Joanne B.; Greenlee, Mark L.; DiNinno, Frank; Huber, Joann L.; Sundelof, Jon G.
CS Department of Medicinal Chemistry, Merck Research Laboratories, Rahway, NJ, 07065, USA
SO Bioorganic & Medicinal Chemistry Letters (1999), 9(20), 2973-2976
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
GI

Q1= 

Q2= 

Q3= 



I

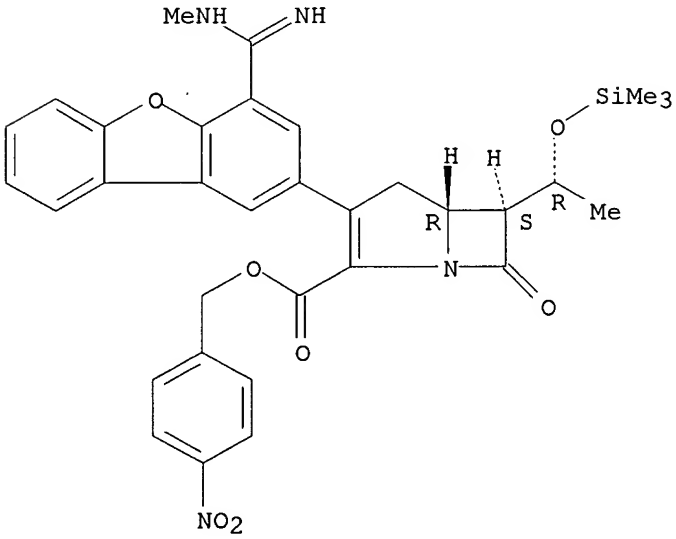
AB A series of amidinium-substituted 2-dibenzofuranylcarbapenem analogs I [R = C(=NH)NH2, C(=NH)NHMe, C(=NH)NMe2, Q1, Q2, Q3 ; R1 = CO2-, CO2H; R2 = H, Me] with potent activity against MRSA has been synthesized via a Stille cross-coupling reaction. I show reduced serum protein binding and improved in vivo efficacy as a consequence of the pos. charged amidinium substituent.

IT **253268-64-3P 253268-65-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and anti-MRSA activity of amidinium-substituted 2-dibenzofuranylcarbapenems)

RN 253268-64-3 CAPLUS

CN 1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 3-[4-[imino(methylamino)methyl]-2-dibenzofuranyl]-7-oxo-6-[(1R)-1-[(trimethylsilyl)oxy]ethyl]-, (4-nitrophenyl)methyl ester, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

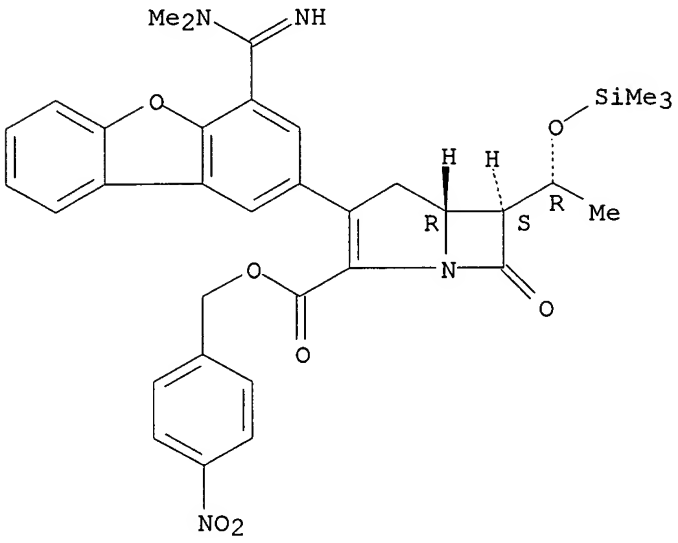


RN 253268-65-4 CAPLUS

CN 1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 3-[4-

[(dimethylamino)iminomethyl]-2-dibenzofuranyl]-7-oxo-6-[(1R)-1-[(trimethylsilyl)oxy]ethyl]-, (4-nitrophenyl)methyl ester, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

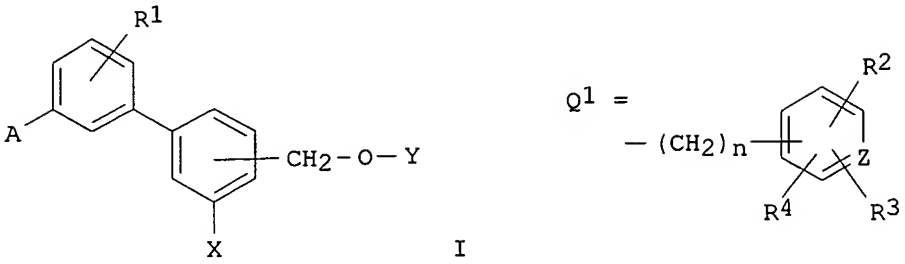


RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:354476 CAPLUS
DN 131:18840
TI Preparation of biphenylamidine derivatives as factor Xa inhibitors
IN Takano, Yasunobu; Nakada, Tomohisa; Hara, Takayuki; Sugiura, Satoshi; Tsutsumi, Takaharu; Takarada, Reiko; Takazawa, Yoshiharu
PA Teijin Limited, Japan
SO PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9926919	A1	19990603	WO 1998-JP5210	19981119
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2310330	AA	19990603	CA 1998-2310330	19981119
	AU 9911741	A1	19990615	AU 1999-11741	19981119
	AU 736112	B2	20010726		
	EP 1043311	A1	20001011	EP 1998-954748	19981119
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	NZ 504324	A	20020201	NZ 1998-504324	19981119
	US 6348478	B1	20020219	US 2000-554449	20000515
	NO 2000002588	A	20000626	NO 2000-2588	20000519

PRAI JP 1997-319696 A 19971120
WO 1998-JP5210 W 19981119
OS MARPAT 131:18840
GI



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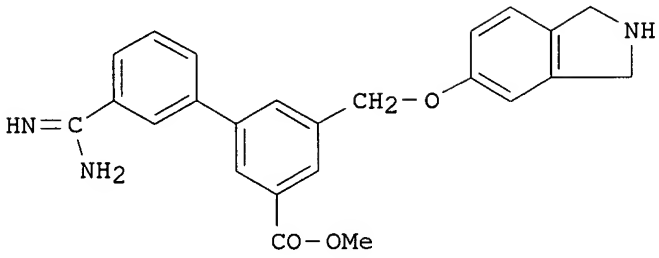


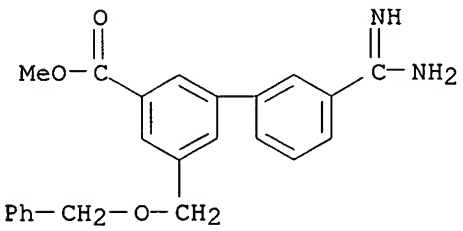
II

AB The title compds. I [A = amidino; R1 = H, amino, nitro, etc.; X = carboxyl, etc.; Y = Q1, etc.; n = 0 -1; Z = CH, N; R2 = H, amino, etc.; R3 = H, alkyl; R4 = H, F, etc.] are prepd. For example, the title compd. II was prepd. Compds. of this invention in vitro showed IC50 of 0.1 .mu.M to 100 .mu.M against factor Xa.

IT **226070-31-1P 226070-32-2P 226070-33-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of biphenylamidine derivs. as factor Xa inhibitors)

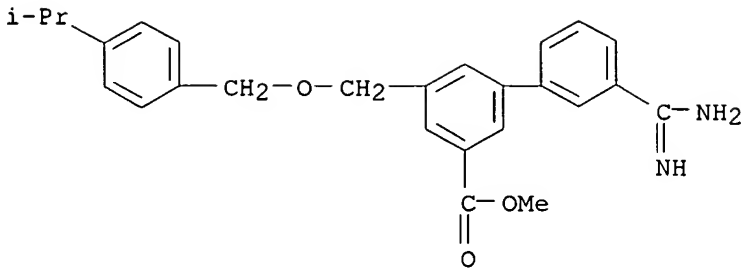
RN 226070-31-1 CAPLUS

CN [1,1'-Biphenyl]-3-carboxylic acid, 3'-(aminoiminomethyl)-5-[(phenylmethoxy)methyl]-, methyl ester (9CI) (CA INDEX NAME)

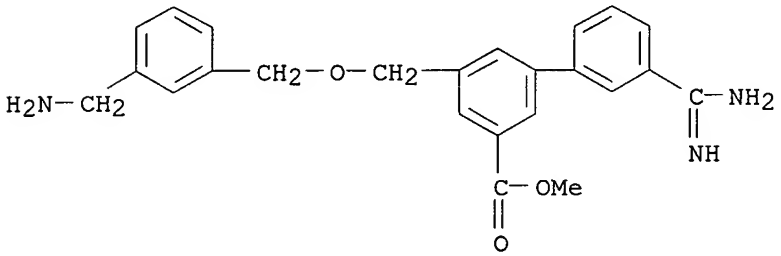


RN 226070-32-2 CAPLUS

CN [1,1'-Biphenyl]-3-carboxylic acid, 3'-(aminoiminomethyl)-5-[[[4-(1-methylethyl)phenyl]methoxy]methyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 226070-33-3 CAPLUS
CN [1,1'-Biphenyl]-3-carboxylic acid, 3'-(aminoiminomethyl)-5-[[[3-(aminomethyl)phenyl]methoxy]methyl]-, methyl ester (9CI) (CA INDEX NAME)

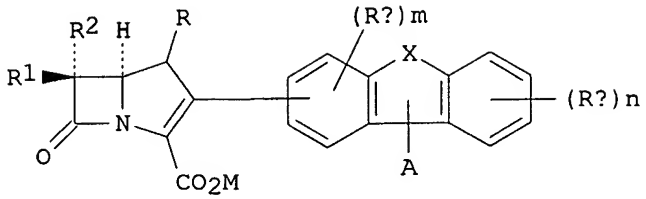


RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:165225 CAPLUS
DN 126:157340
TI Preparation of 2-(dibenzofuranyl)- and 2-(dibenzothienyl)-carbapenems for use as antibiotics
IN Greenlee, Mark L.; Laub, Joanne B.
PA Merck and Co., Inc., USA
SO Brit. UK Pat. Appl., 77 pp.
CODEN: BAXXDU
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB 2301820	A1	19961218	GB 1996-11166	19960529
PRAI US 1995-476302		19950607		

OS MARPAT 126:157340
GI



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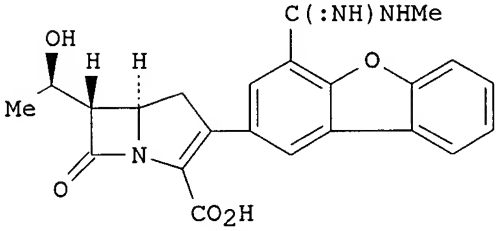

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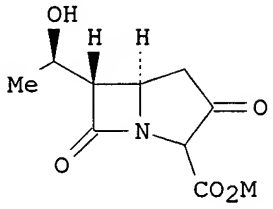


III

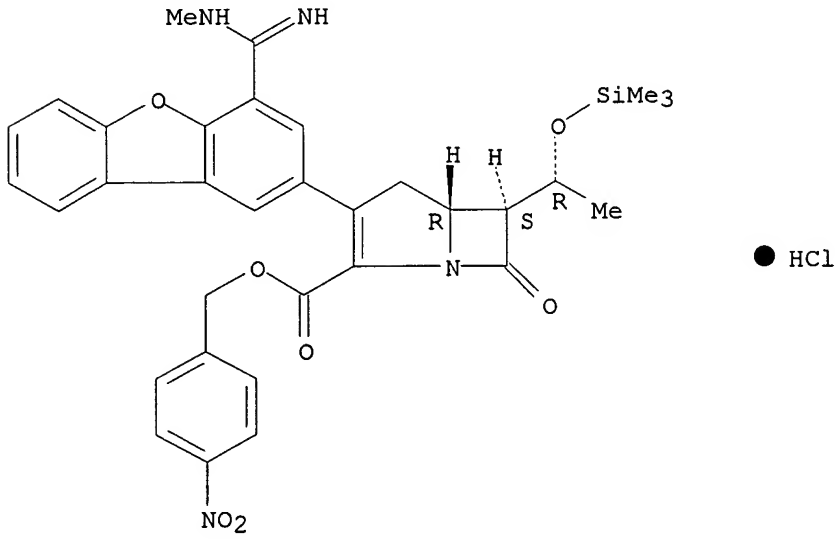
AB Carbapenem compds. I [R = H or CH3; R1 and R2 = independently H, Me, Et, (Me)2CH, HOCH2, MeCH(OH), (Me)2C(OH), FCH2CH(OH), F2CHCH(OH), F3CCH(OH), MeCF2, or (Me)2C(F); X = O, S, S(O) or S(O)2; A = carboximidamide, 1-imidazolium, 1-pyridinium, 2-pyrimidinyl; Rc = substituent such as alkyloxy, alkylthio, tetrazolyl, halo, haloalkyl, OH, carbamoyloxy, amino, acyl; m and n = independently an integer from 0 to 4; M = H, alkali metal, ester, ester protecting group] were prepd. for use as antibiotics (no data). Thus, carbapenem II was prepd. via a series of synthetic steps starting from 2-bromo-4-dibenzofurancarboxaldehyde and ADC-13 (III; M = 4-NO2C6H4CH2) as the principle starting materials.

IT **186821-90-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 2-(dibenzofuranyl)- and 2-(dibenzothienyl)-carbapenems for use as antibiotics)

RN 186821-90-9 CAPLUS

CN 1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 3-[4-[imino(methylamino)methyl]-2-dibenzofuranyl]-7-oxo-6-[1-[(trimethylsilyl)oxy]ethyl]-, (4-nitrophenyl)methyl ester, monohydrochloride, [5R-[5.alpha.,6.alpha.(R*)]]- (9CI) (CA INDEX NAME)

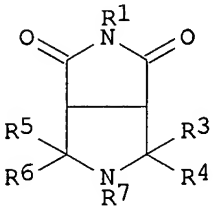
Absolute stereochemistry.



L20 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:623064 CAPLUS
DN 125:275852
TI Preparation of dioxopyrrolopyrrole antithrombotics and blood platelet aggregation inhibitors
IN Diederich, Francois; Obst, Ulrike; Wallbaum, Sabine; Weber, Lutz
PA F. Hoffmann-La Roche Ag, Switz.
SO Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 728758	A1	19960828	EP 1996-102446	19960219
	EP 728758	B1	20031015		
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL				
	JP 08245624	A2	19960924	JP 1996-33395	19960221
	JP 2885682	B2	19990426		
	CN 1136567	A	19961127	CN 1996-102534	19960226
	CN 1056844	B	20000927		
	US 5686459	A	19971111	US 1996-606811	19960226
PRAI	CH 1995-552	A	19950227		
	CH 1995-3457	A	19951207		

OS MARPAT 125:275852
GI



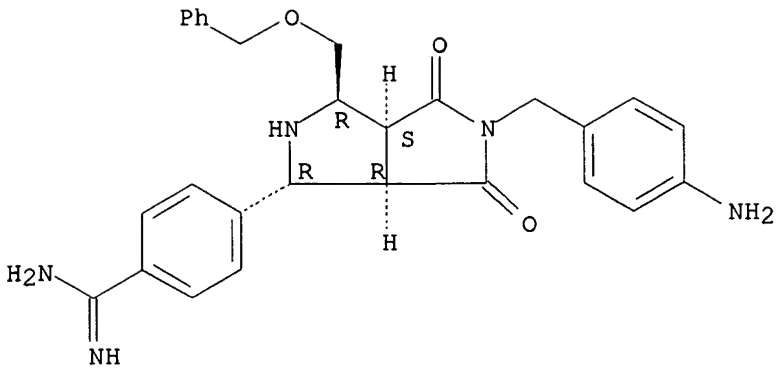
I

AB The title compds. [I; R1, R2 = H, (un)substituted alkyl (hetero)aryl, cycloalkyl, etc.; R3 = H, CO2H, (un)substituted CONH2, etc.; R4-R6 = H, alkyl, aryl, aralkyl, cycloalkyl] [e.g., (3aRS,4SR,8aRS,8bSR)-4-(2-benzyl-1,3-dioxodecahydropyrrolo[3,4-a]pyrrolizin-4-yl)benzamide hydrochloride; m.p. 202-205.degree.; IC50 0.22 .mu.M against the amidolytic activity of thrombin], useful as antithrombotics and blood platelet aggregation inhibitors, are prepd. and I-contg. formulations presented.

IT **182189-28-2P 182190-83-6P 182268-81-1P**
182268-89-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of dioxopyrrolopyrrole antithrombotics and blood platelet aggregation inhibitors)

RN 182189-28-2 CAPLUS
CN Benzenecarboximidamide, 4-[5-[(4-aminophenyl)methyl]octahydro-4,6-dioxo-3-[(phenylmethoxy)methyl]pyrrolo[3,4-c]pyrrol-1-yl]-, monohydrochloride, (1.alpha.,3.beta.,3a.alpha.,6a.alpha.)- (9CI) (CA INDEX NAME)

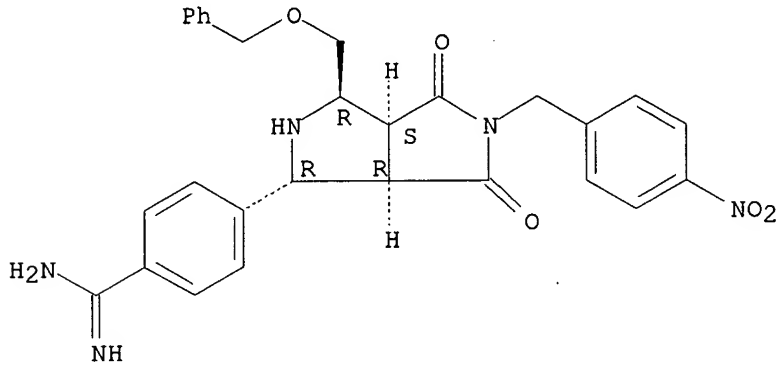
Relative stereochemistry.



● HCl

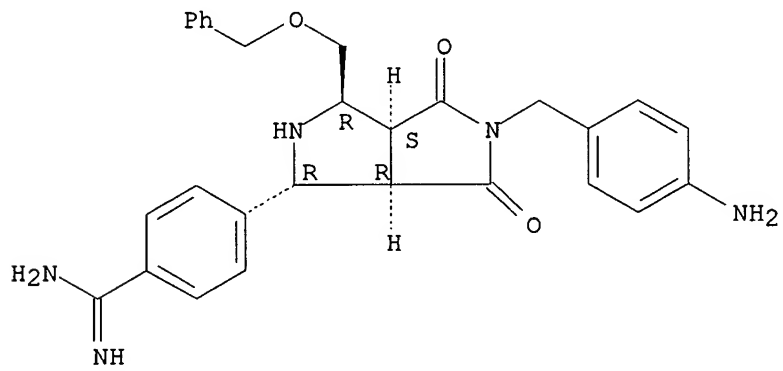
RN 182190-83-6 CAPLUS
CN Benzenecarboximidamide, 4-[octahydro-5-[(4-nitrophenyl)methyl]-4,6-dioxo-3-[(phenylmethoxy)methyl]pyrrolo[3,4-c]pyrrol-1-yl]-, (1.alpha.,3.beta.,3a.alpha.,6a.alpha.)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



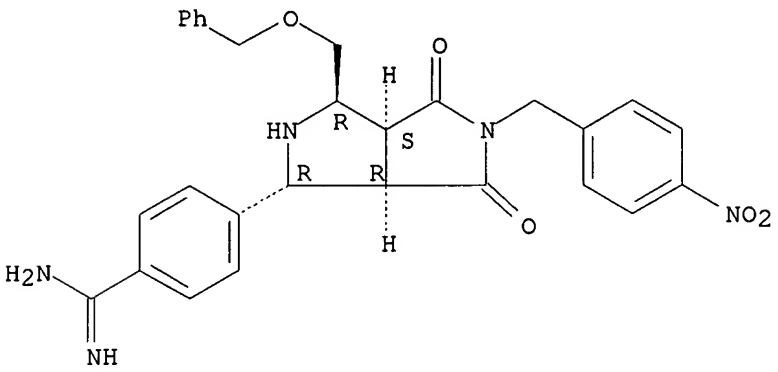
RN 182268-81-1 CAPLUS
CN Benzenecarboximidamide, 4-[[5-(4-aminophenyl)methyl]octahydro-4,6-dioxo-3-[(phenylmethoxy)methyl]pyrrolo[3,4-c]pyrrol-1-yl]-, (1.alpha.,3.beta.,3a.alpha.,6a.alpha.)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



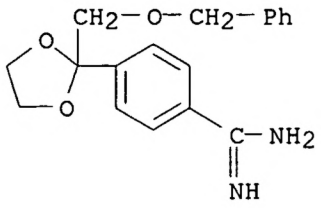
RN 182268-89-9 CAPLUS
CN Benzenecarboximidamide, octahydro-4-[[5-(4-nitrophenyl)methyl]-4,6-dioxo-3-[(phenylmethoxy)methyl]pyrrolo[3,4-c]pyrrol-1-yl]-, monohydrochloride, (1.alpha.,3.beta.,3a.alpha.,6a.alpha.)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

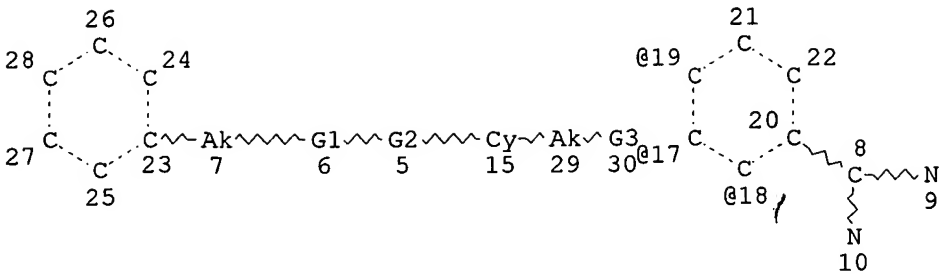


● HCl

L20 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1976:542770 CAPLUS
DN 85:142770
TI Synthesis of amidinophenyl aryl ketones and .alpha.-substituted amidinoacetophenones
AU Wagner, G.; Voigt, B.; Steinbrueck, K.
CS Sekt. Biowiss., Karl-Marx-Univ., Leipzig, Ger. Dem. Rep.
SO Pharmazie (1976), 31(6), 354-60
CODEN: PHARAT; ISSN: 0031-7144
DT Journal
LA German
AB 4-RC6H4COC6H4C(:NH)NH2.HCl-3(or 4) (R = H, Me, Cl, OMe, Ph, OPh) were mostly prepd. by the Friedel-Crafts acylation of RPh with 3- or 4-NCC6H4COCl (I), followed by the Pinner reaction. 4-PhCH2COC6H4C(:NH)NH2.HCl was prepd. by the acylation of PhCH(CO2Me)2 with I, followed by sapon., decarboxylation, and Pinner reaction. 4-RCH2CH2COC6H4C(:NH)NH2.HCl (R = Ph, 1-C10H7) were prepd. by the condensation of 4-NCC6H4COMe with PhCHO or 1-C10H7CHO, hydrogenation of the resulting 1,3-diaryl-2-propen-1-one, and Pinner reaction.
IT **60695-18-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 60695-18-3 CAPLUS
CN Benzenecarboximidamide, 4-[2-[(phenylmethoxy)methyl]-1,3-dioxolan-2-yl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl



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REP G2=(0-3) CH2
VAR G3=19/18/17
ENTER (DIS), GRA, NOD, BON OR ?:end
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SAMPLE SCREEN SEARCH COMPLETED - 3487 TO ITERATE

28.7% PROCESSED 1000 ITERATIONS 2 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 66200 TO 73280
PROJECTED ANSWERS: 2 TO 297

L5 2 SEA SSS SAM L4

=> d 1-2

L5 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2003 ACS on STN
RN 326861-99-8 REGISTRY
CN 1H-Benzimidazole-5-carboxamide, N-(2-aminoethyl)-2-[2-[4-(aminoiminomethyl)phenyl]ethyl]-N-[(3-methoxyphenyl)methyl]-1-(2-phenylethyl)- (9CI) (CA INDEX NAME)
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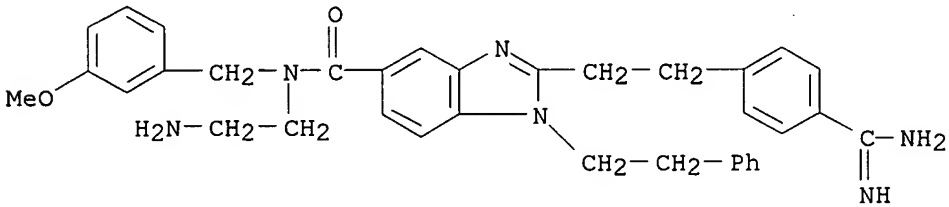
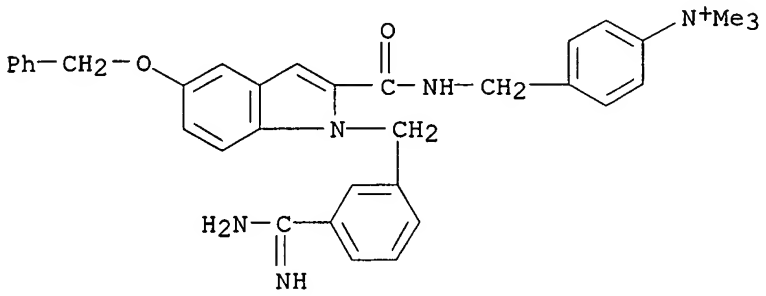
MF C35 H38 N6 O2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2003 ACS on STN
RN 229951-25-1 REGISTRY
CN Benzenaminium, 4-[[[[1-[[3-(aminoiminomethyl)phenyl]methyl]-5-(phenylmethoxy)-1H-indol-2-yl]carbonyl]amino]methyl]-N,N,N-trimethyl-(9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C34 H36 N5 O2
CI COM
SR CA



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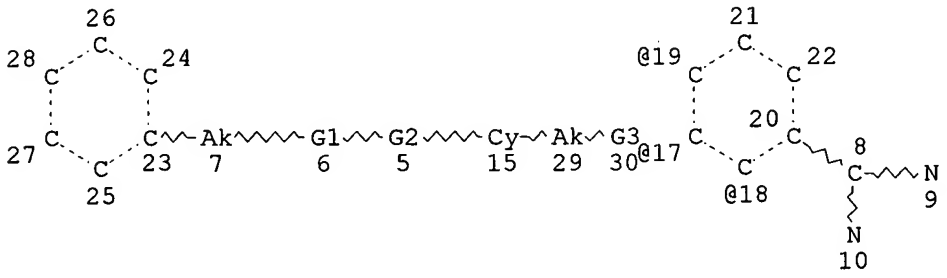

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REP G2=(0-3) CH2
VAR G3=19/18/17
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE

=> s l4 ful
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L6 95 SEA SSS FUL L4

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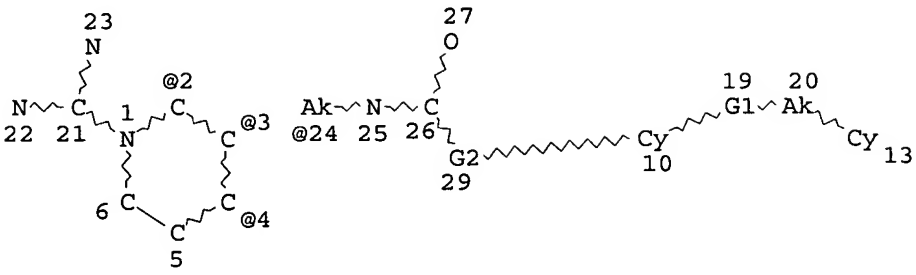
L15 STR



VAR G1=O/S/N
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VPA 24-2/3/4 U
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 3
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE

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FULL SCREEN SEARCH COMPLETED - 6395 TO ITERATE

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SEARCH TIME: 00.00.01

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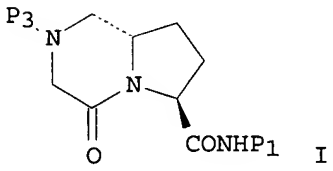
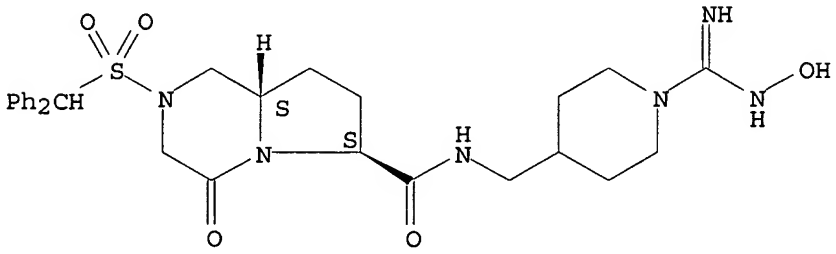
L19 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 2002:251344 CAPLUS
DN 137:332728
TI Novel bicyclic lactam inhibitors of thrombin: highly potent and selective inhibitors
AU St-Denis, Yves; Levesque, Sophie; Bachand, Benoit; Edmunds, Jeremy J.; Leblond, Lorraine; Preville, Patrice; Tarazi, Micheline; Winocour, Peter D.; Siddiqui, M. Arshad
CS Shire BioChem., Laval, QC, H7V 4A7, Can.
SO Bioorganic & Medicinal Chemistry Letters (2002), 12(8), 1181-1184
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
GI



I

AB The potency and selectivity of a previous series of low mol. wt. thrombin inhibitors were improved through modifications of the P1 and P3 residues in the formula I. Introduction of di-Ph substituted sulfonamides in the P3 moiety led to highly efficacious compds. By correctly selecting the combination of P1 and P3 residues, high levels of potency, selectivity and in vivo efficacy were obtained.
IT **325690-68-4P 473923-12-5P 473923-15-8P**
473923-32-9P 473923-50-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and structure activity relations of bicyclic lactams as novel highly potent and selective thrombin inhibitors)
RN 325690-68-4 CAPLUS
CN Pyrrolo[1,2-a]pyrazine-6-carboxamide, 2-[(diphenylmethyl)sulfonyl]octahydro-N-[[1-[(hydroxyamino)iminomethyl]-4-piperidinyl]methyl]-4-oxo-, (6S,8aS)- (9CI) (CA INDEX NAME)

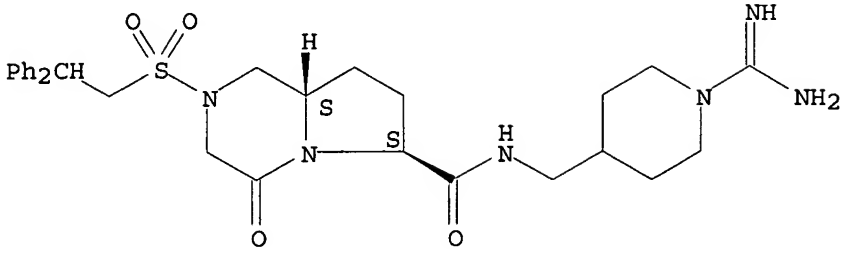
Absolute stereochemistry.



RN 473923-12-5 CAPLUS
CN Pyrrolo[1,2-a]pyrazine-6-carboxamide, N-[[1-(aminoiminomethyl)-4-piperidinyl]methyl]-2-[(2,2-diphenylethyl)sulfonyl]octahydro-4-oxo-,

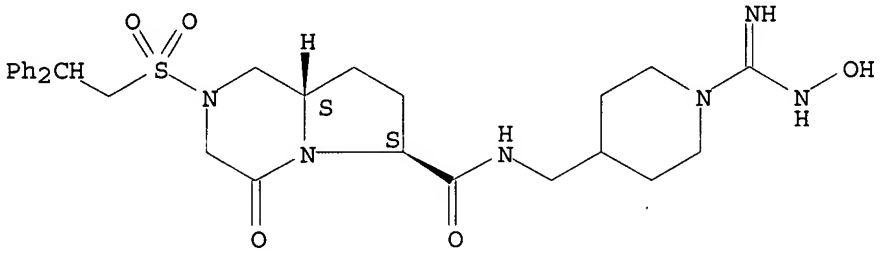
(6S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



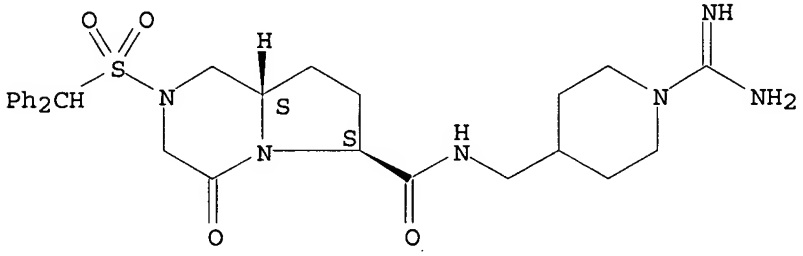
RN 473923-15-8 CAPLUS
CN Pyrrolo[1,2-a]pyrazine-6-carboxamide, 2-[(2,2-diphenylethyl)sulfonyl]octahydro-N-[[1-[(hydroxyamino)iminomethyl]-4-piperidinyl]methyl]-4-oxo-, (6S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



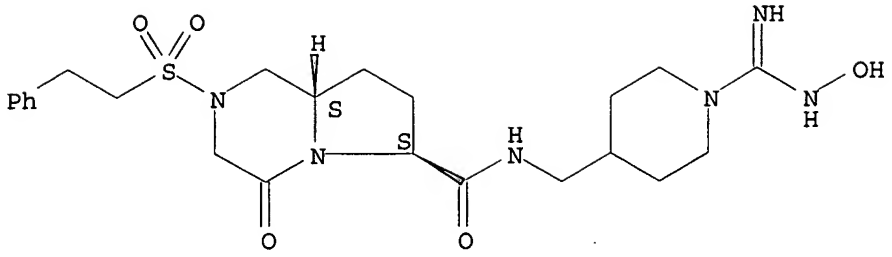
RN 473923-32-9 CAPLUS
CN Pyrrolo[1,2-a]pyrazine-6-carboxamide, N-[[1-(aminoiminomethyl)-4-piperidinyl]methyl]-2-[(diphenylmethyl)sulfonyl]octahydro-4-oxo-, (6S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 473923-50-1 CAPLUS
CN Pyrrolo[1,2-a]pyrazine-6-carboxamide, octahydro-N-[[1-[(hydroxyamino)iminomethyl]-4-piperidinyl]methyl]-4-oxo-2-[(2-phenylethyl)sulfonyl]-, (6S,8aS)- (9CI) (CA INDEX NAME)

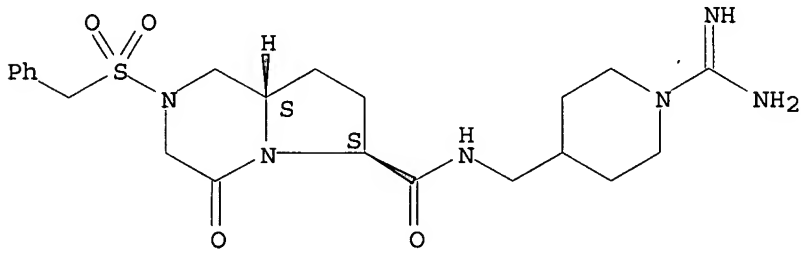
Absolute stereochemistry.



RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

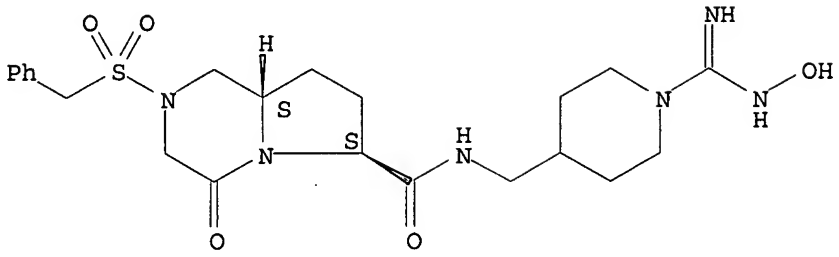
L19 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 2001:872229 CAPLUS
DN 136:210039
TI Novel bicyclic lactam inhibitors of thrombin: potency and selectivity optimization through P1 residues
AU Levesque, Sophie; St. Denis, Yves; Bachand, Benoit; Preville, Patrice; Leblond, Lorraine; Winocour, Peter D.; Edmunds, Jeremy J.; Rubin, J. R.; Siddiqui, M. Arshad
CS Shire BioChem Inc., Laval, QC, H7V 4A7, Can.
SO Bioorganic & Medicinal Chemistry Letters (2001), 11(24), 3161-3164
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB Peptidomimetic inhibitors of thrombin lacking the important Ser195-carbonyl interaction have been prepd. The binding energy lost after the removal of the activated carbonyl was recaptured through a series of modifications of the P1 residues of the bicyclic lactam inhibitors. Selected substituted compds. displayed useful pharmacol. profiles both in vitro and in vivo.
IT **401947-02-2P 401947-05-5P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of novel peptidomimetic bicyclic lactam inhibitors of thrombin and their potency and selectivity optimization through P1 residues)
RN 401947-02-2 CAPLUS
CN Pyrrolo[1,2-a]pyrazine-6-carboxamide, N-[[1-(aminoiminomethyl)-4-piperidinyl]methyl]octahydro-4-oxo-2-[(phenylmethyl)sulfonyl]-, (6S,8aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 401947-05-5 CAPLUS
CN Pyrrolo[1,2-a]pyrazine-6-carboxamide, octahydro-N-[[1-[(hydroxyamino)iminomethyl]-4-piperidinyl]methyl]-4-oxo-2-[(phenylmethyl)sulfonyl]-, (6S,8aS)- (9CI) (CA INDEX NAME)

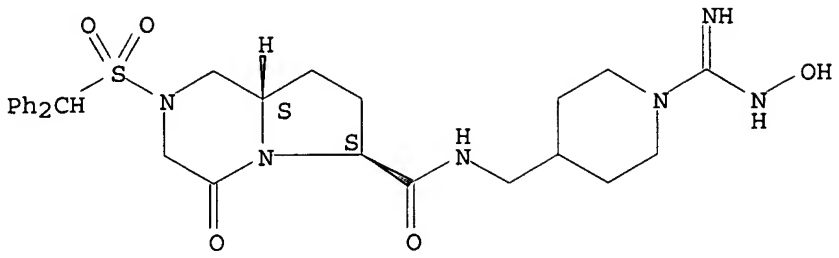
Absolute stereochemistry.



RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 2000:853514 CAPLUS
DN 134:157368
TI In Vitro and in Vivo Properties of Bicyclic Lactam Inhibitors. A Novel Class of Low Molecular Weight Peptidomimetic Thrombin Inhibitors
AU Leblond, L.; Grouix, B.; Boudreau, C.; Yang, Q.; Siddiqui, M. A.; Winocour, P. D.
CS BioChem Pharma Inc., Laval, QC, H7V 4A7, Can.
SO Thrombosis Research (2000), 100(3), 195-209
CODEN: THBRAA; ISSN: 0049-3848
PB Elsevier Science Inc.
DT Journal
LA English
AB We have developed potent and selective thrombin inhibitors with a novel non-peptidic structure. A bicyclic lactam was used as the scaffold on which various P1 and P3 motifs were substituted. Herein, we report the in vitro and in vivo properties of four representatives of this novel class of inhibitors. Their Ki values were less than 10 nM, they inhibited equally both free and clot-bound thrombin, and they displayed high level of specificity for thrombin over other serine proteases (trypsin, factor Xa, activated Protein C, and plasmin). They prolonged the clotting time of human plasma to twice the control value in coagulation assays (TT, APTT, and PT) at a concn. below 3 .mu.M. Their anticoagulant activities using rat plasma were similar to, although slightly weaker, than with human plasma. Furthermore, they inhibited thrombin-induced platelet aggregation (human and rat) at concns. close to their Ki values for thrombin. These mols. demonstrated similar dose response antithrombotic efficacy in rat arterial and venous thrombosis models when given as i.v. bolus followed by infusion. Antithrombotic efficacy of 85% and greater was obsd. at a dose of 5-7 .mu.M/kg/h in each model. Bicyclic lactam inhibitor 3, at a dose which caused a complete inhibition of visible thrombus formation in the venous and arterial models of thrombosis, showed a 1.9-2.1 and a 4.0-4.8-fold shift in APTT and TT, resp. Unfortunately, the bicyclic lactam inhibitors exhibited low oral bioavailability in rats. Therefore, this novel class of bicyclic lactam thrombin inhibitor has the potential to be promising i.v. antithrombotic agents for the treatment of arterial as well as venous thrombosis and warrants further investigation.
IT **325690-68-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bicyclic lactams with specificity for thrombin inhibition over other serine proteases)
RN 325690-68-4 CAPLUS
CN Pyrrolo[1,2-a]pyrazine-6-carboxamide, 2-[(diphenylmethyl)sulfonyl]octahydro-N-[[1-[(hydroxyamino)iminomethyl]-4-piperidinyl]methyl]-4-oxo-, (6S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

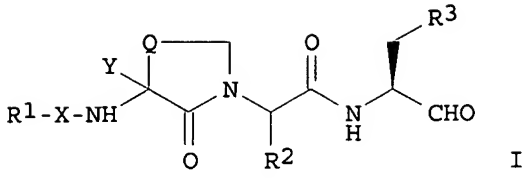


RE.CNT 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1999:487130 CAPLUS
DN 131:116524
TI 3-Amino-2-oxo-1-piperidineacetic derivatives containing an arginine mimic as enzyme inhibitors
IN Semple, Joseph E.; Levy, Odile E.; Nutt, Ruth F.; Ripka, William C.
PA Corvas International, Inc., USA
SO U.S., 38 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5932733	A	19990803	US 1995-482117	19950607
	US 5714499	A	19980203	US 1994-261498	19940617
	CA 2192211	AA	19951228	CA 1995-2192211	19950619
	WO 9535313	A1	19951228	WO 1995-US7832	19950619
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9529054	A1	19960115	AU 1995-29054	19950619
	EP 765339	A1	19970402	EP 1995-924623	19950619
	EP 765339	B1	19990127		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 10503177	T2	19980324	JP 1995-502570	19950619
	AT 176241	E	19990215	AT 1995-924623	19950619
PRAI	US 1994-261498		19940617		
	US 1994-356831		19941213		
	US 1995-482117		19950607		
	WO 1995-US7832		19950619		

OS MARPAT 131:116524
GI



I

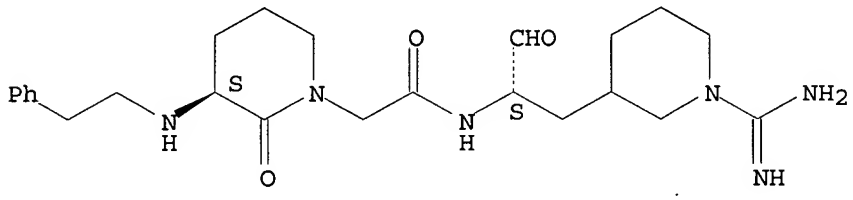
AB Peptide aldehydes I [X = SO2, NR'SO2 (R' = H, alkyl, aryl, aralkyl), CO, O2C, NHCO, P(O)R'' (R'' = NR', OR', R', SR', where R' .noteq. H), direct link; R1 = (un)substituted alkyl, cycloalkyl, heterocycloalkyl, alkenyl, aryl, etc.; Q = (CH2)n (n = 1-4), (CH2)qR4 [q = 1, 2; R4 = S(O)p (p = 0-2), O, NR5 (R5 = H, alkyl, aryl)]; R2 = H, alkyl, alkenyl; R3 = 3-amidinocyclohexyl or -Ph, 1-amidino-3-piperidyl; Y is selected from R1 substituents, but not certain aza heterocycles] and their pharmaceutically acceptable salts were prepd. as thrombin inhibitors. Thus, benzylsulfonyl-norval(cyclo)-Gly-3-[3-piperidyl(N-guanidino)]-L-alaninal was prepd. as a mixt. of diastereomers. Isomer B showed inhibition const. Ki = 0.318 .+-. 16 nM against human .alpha.-thrombin amidolytic activity.

IT **232608-28-5P 232608-31-0P 232608-34-3P**
232608-37-6P 232608-40-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aminooxopiperidineacetic derivs. contg. an arginine mimic as enzyme inhibitors)

RN 232608-28-5 CAPLUS

CN 1-Piperidineacetamide, N-[(1S)-2-[1-(aminoiminomethyl)-3-piperidinyl]-1-formylethyl]-2-oxo-3-[(2-phenylethyl)amino]-, (3S)- (9CI) (CA INDEX NAME)

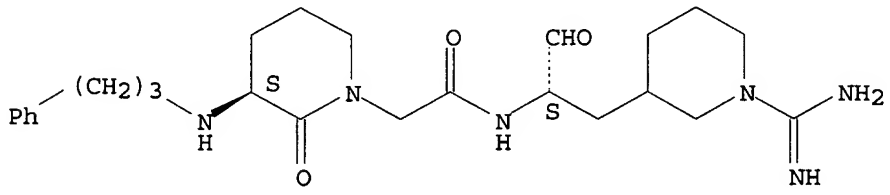
Absolute stereochemistry.



RN 232608-31-0 CAPLUS

CN 1-Piperidineacetamide, N-[(1S)-2-[1-(aminoiminomethyl)-3-piperidinyl]-1-formylethyl]-2-oxo-3-[(3-phenylpropyl)amino]-, (3S)- (9CI) (CA INDEX NAME)

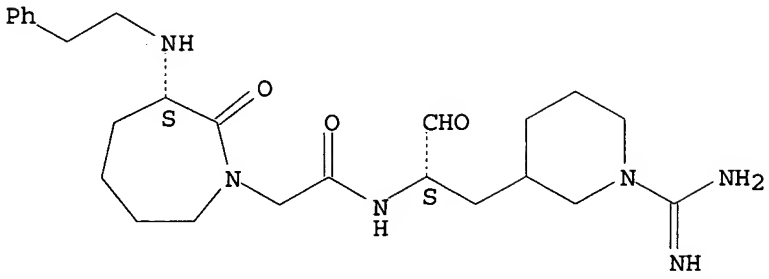
Absolute stereochemistry.



RN 232608-34-3 CAPLUS

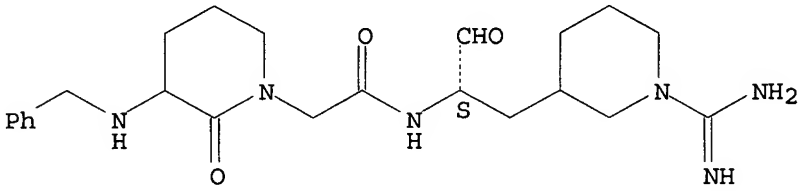
CN 1H-Azepine-1-acetamide, N-[(1S)-2-[1-(aminoiminomethyl)-3-piperidinyl]-1-formylethyl]hexahydro-2-oxo-3-[(2-phenylethyl)amino]-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



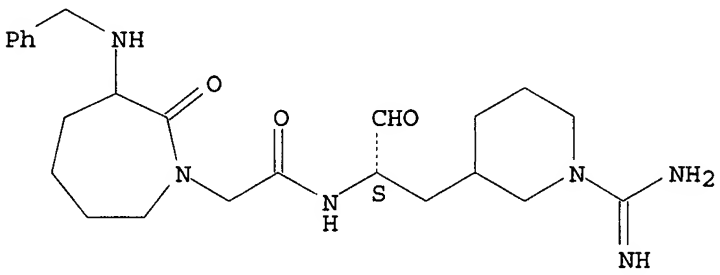
RN 232608-37-6 CAPLUS
CN 1-Piperidineacetamide, N-[(1S)-2-[1-(aminoiminomethyl)-3-piperidinyl]-1-formylethyl]-2-oxo-3-[(phenylmethyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 232608-40-1 CAPLUS
CN 1H-Azepine-1-acetamide, N-[(1S)-2-[1-(aminoiminomethyl)-3-piperidinyl]-1-formylethyl]hexahydro-2-oxo-3-[(phenylmethyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



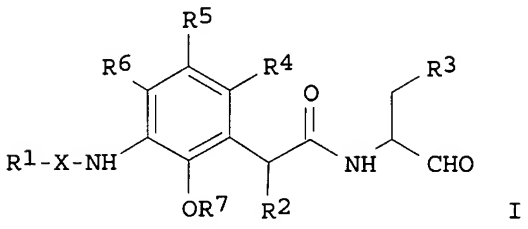
RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1999:354477 CAPLUS
DN 130:352556
TI Synthesis of substituted 3-amino-2-hydroxyphenylacetamide derivatives as enzyme inhibitors
IN Semple, Joseph Edward; Lim-Wilby, Marguerita S.; Brunck, Terence K.
PA Corvas International, Inc., USA
SO PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9926920	A1	19990603	WO 1998-US25167	19981123
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6011047	A	20000104	US 1997-980114	19971126
	US 6204384	B1	20010320	US 1997-979440	19971126
	AU 9916056	A1	19990615	AU 1999-16056	19981123
PRAI	US 1997-979440	A	19971126		
	US 1997-980114	A	19971126		
	WO 1998-US25167	W	19981123		

OS MARPAT 130:352556

GI



I

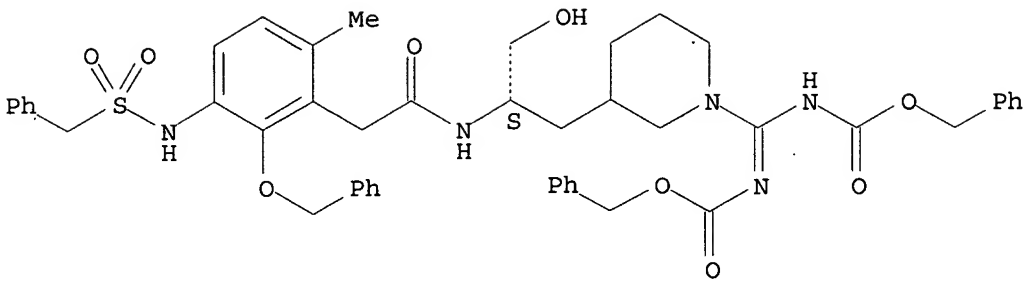
AB Peptide aldehydes I [X = SO2, NR'SO2, CO, OCO, NHCO, P(O)R'', or direct link (R' = H, alkyl, aryl, aralkyl; R'' = NHR', OR', R', SR'); R1 = (un)substituted alkyl, cycloalkylalkyl, cycloalkyl, heterocycloalkyl, aryl, etc.; R2 = H, alkyl, alkenyl; R3 = HN:C(NH2)NH(CH2)d (d = 0-5), 3- or 4-guanylcyclohexyl, 1-guanyl-3- or -4-piperidinyl; m- or p-guanylphenyl; R4, R5, R6 = R1, OR1, NHR1, SR1, S(O)R1, CF3, CF2H, OCF3, OCF2H, halo, etc.; R7 = R1, CF3, CF2H, etc.] were prepd. as enzyme inhibitors. Thus, N-[[2-hydroxy-3-(benzylsulfonylamino)-6-methylphenyl]acetyl]-L-argininal (in cyclol form) trifluoroacetate was prepd. and showed IC50 = 3.19 nM for inhibition of thrombin.

IT **225096-40-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of substituted aminohydroxyphenylacetamide derivs. as enzyme inhibitors)

RN 225096-40-2 CAPLUS

CN Carbamic acid, [[3-[(2S)-3-hydroxy-2-[[[6-methyl-2-(phenylmethoxy)-3-[[(phenylmethyl)sulfonyl]amino]phenyl]acetyl]amino]propyl]-1-piperidinyl][[(phenylmethoxy)carbonyl]amino]methylene]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1998:479552 CAPLUS
DN 129:109333
TI Preparation of heterobicyclic peptide derivatives as thrombin inhibitors
IN Bachand, Benoit; Doherty, Annette Marian; Siddiqui, M. Arshad; Edmunds, Jeremy John
PA Biochem Pharma Inc., Can.
SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9828326	A1	19980702	WO 1997-US22985	19971222
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9855260	A1	19980717	AU 1998-55260	19971222
PRAI	US 1996-34311P	P	19961223		
	WO 1997-US22985	W	19971222		

OS MARPAT 129:109333
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB This invention relates to heterobicyclic peptide derivs. I [A = (CHR8)0-1, S, S(O), SO2, NR8; B = S, SO2, O, N, NH, CH, CR6R7; D = (CHR9)0-2, CH; E = CH2, CHCOR9; X = O, NR5, CHR5; Y = O, S, S(O), SO2, NR5, CO, CHR8; Z = O, S, H2; R1 = any group Q-Q3; J = CH, N; K = bond, NH, G = C1-4 alkoxy, CN, NH2, CH2NH2, C(NH2):NH, NHC(NH2):NH, CH2NHC(NH2):NH, etc; U = CN, NH2, C(NH2):NH, NHC(NH2):NH; T = H, OH, amino, peptide residue contg. 1-4 amino acids, C1-6 alkyl, C1-16 alkoxy, C6-20 aralkyl, C6-16 aryloxy, C6-20 arylalkoxy, (un)substituted aryl or heterocycle; R2 = H, (un)substituted C1-6 alkyl; R3 = H, NR6R7, C1-6 alkyl; R4, R5 = independently H, NR6R7, C6-16 aryl, (un)substituted C3-7 cycloalkyl, (un)substituted, optionally heteroatom-interrupted C1-6 alkyl; R6, R7 = independently H, C1-6 alkyl; R8 = H, optionally heteroatom-interrupted C1-6 alkyl, C6-16 aryl, C3-7 cycloalkyl, heterocyclyl, hydrophobic group; R9 = H, C1-6 alkyl, COR1; R11 = H, C1-6 alkyl], their prepn., and pharmaceutical compns. thereof, as

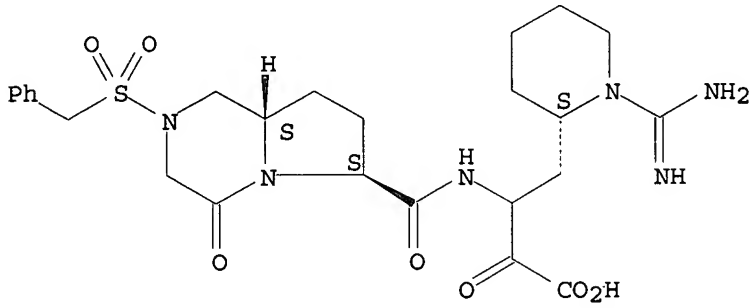
thrombin inhibitors. Also, the invention relates to the use of such compds. and compns. as anticoagulants and as agents for the treatment and prophylaxis of thrombotic disorders such as venous thrombosis, pulmonary embolism and arterial thrombosis resulting in acute ischemic events such as myocardial infarction or cerebral infarction. Thus, amidation of keto ester II (Mtr = 4-methoxy-2,3,6-trimethylbenzenesulfonyl) (prepn. given) with octahydropyrrolo[1,2-a]pyrazinecarboxylic acid III, followed by sapon. and acidic deprotection gave inhibitor IV as a trifluoroacetate salt. IV inhibited human .alpha.-thrombin with Ki = 0.09 nM in an in vitro assay.

IT **209796-67-8P 209796-68-9P 209796-71-4P 209796-72-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heterobicyclic peptide derivs. as thrombin inhibitors)

RN 209796-67-8 CAPLUS

CN 2-Piperidinebutanoic acid, 1-(aminoiminomethyl)-.beta.-[[[(6S,8aS)-octahydro-4-oxo-2-[(phenylmethyl)sulfonyl]pyrrolo[1,2-a]pyrazin-6-yl]carbonyl]amino]-.alpha.-oxo-, (2S)- (9CI) (CA INDEX NAME)

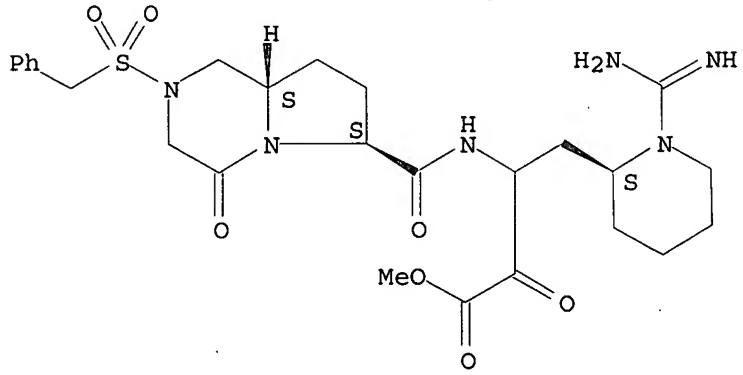
Absolute stereochemistry.



RN 209796-68-9 CAPLUS

CN 2-Piperidinebutanoic acid, 1-(aminoiminomethyl)-.beta.-[[[(6S,8aS)-octahydro-4-oxo-2-[(phenylmethyl)sulfonyl]pyrrolo[1,2-a]pyrazin-6-yl]carbonyl]amino]-.alpha.-oxo-, methyl ester, (2S)- (9CI) (CA INDEX NAME)

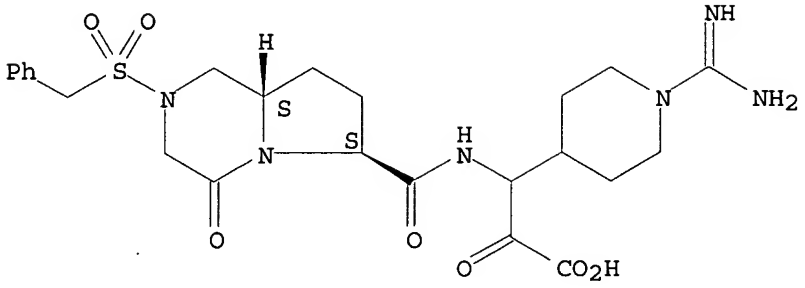
Absolute stereochemistry.



RN 209796-71-4 CAPLUS

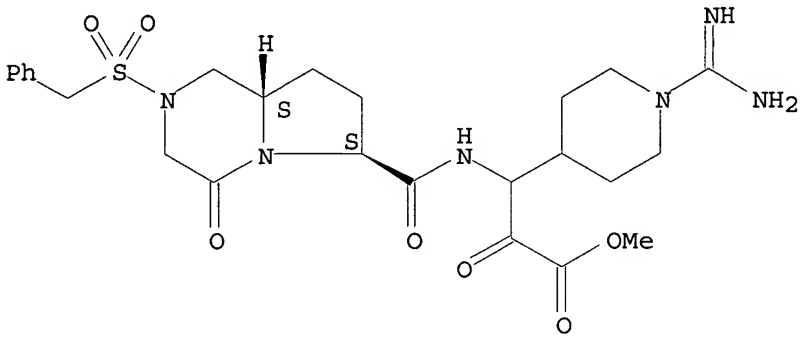
CN 4-Piperidinepropanoic acid, 1-(aminoiminomethyl)-.beta.-[[[(6S,8aS)-octahydro-4-oxo-2-[(phenylmethyl)sulfonyl]pyrrolo[1,2-a]pyrazin-6-yl]carbonyl]amino]-.alpha.-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 209796-72-5 CAPLUS
CN 4-Piperidinepropanoic acid, 1-(aminoiminomethyl)-.beta.-[[[(6S,8aS)-octahydro-4-oxo-2-[(phenylmethyl)sulfonyl]pyrrolo[1,2-a]pyrazin-6-yl]carbonyl]amino]-.alpha.-oxo-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1998:175945 CAPLUS
DN 128:244342
TI Preparation of lactam inhibitors of thrombin
IN St. Denis, Yves; Siddiqui, M. Arshad; Cody, Wayne Livingston; Edmunds, Jeremy John; Plummer, Janet Samartino
PA Biochem Pharma, Inc., Can.; St-Denis, Yves; Siddiqui, M. Arshad; Cody, Wayne Livingston; Edmunds, Jeremy John; Plummer, Janet Samartino
SO PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

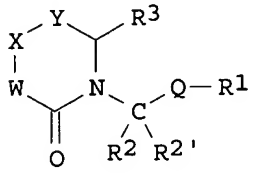
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9809987	A1	19980312	WO 1997-US15312	19970905

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

	AU 9741723	A1	19980326	AU 1997-41723	19970905
PRAI	GB 1996-18687	A	19960906		
	US 1996-25599P	P	19960906		
	WO 1997-US15312	W	19970905		

OS MARPAT 128:244342

GI



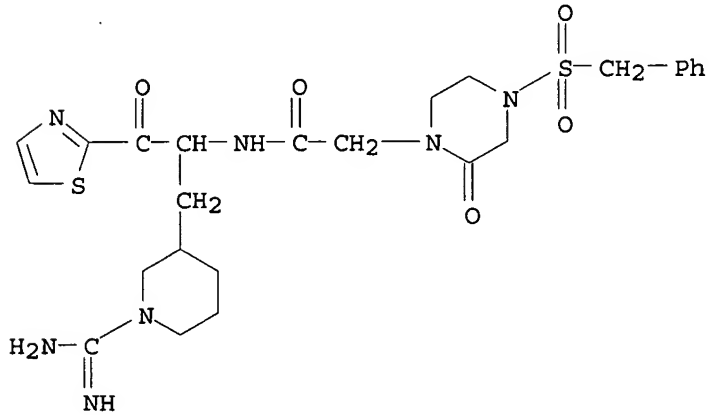
I

AB Heterocyclic thrombin inhibitors I (W, X = CHR4, CR4, NR4, N, O, S, SO, SO2, provided that at least one of W and X is NR4, N, O, S, SO, SO2; Y = CHR4, CR4, CO; Q = CO, CS, CHR4; R1 is a polar amino acid residue or deriv. or analog optionally substituted with an amino acid, peptide, or heterocycle; R2, R2' = H, halo, or alkyl optionally substituted by an aryl, heterocyclic or cycloalkyl group; R3, R4 = H, NH2, alkylamino, CO2H, aryl, cycloalkyl, etc.) were prepd. Thus, N-[4-guanidino-1-(thiazole-2-carbonyl)butyl]-2-[2-oxo-4-(3-phenylpropionyl)-1-piperazinyl]acetamide, prepd. by a coupling procedure in which the guanidino group is protected by 4-methoxy-2,3,6-trimethylbenzenesulfonyl, was assayed for thrombin affinity (IC50 = 35 nM).

IT **204690-44-8P 204690-48-2P 204690-49-3P**
204691-55-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of lactam inhibitors of thrombin)

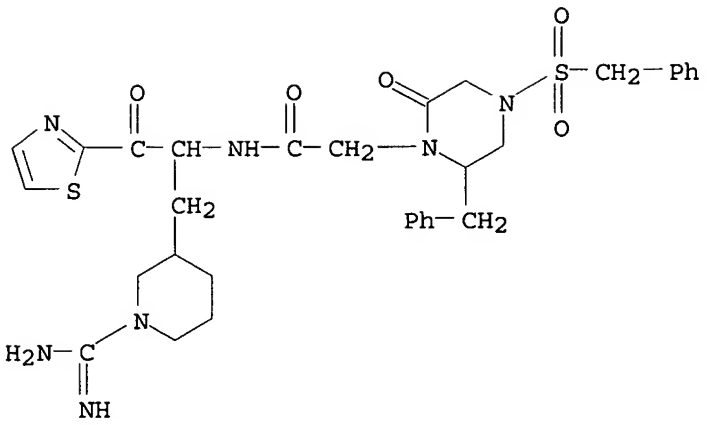
RN 204690-44-8 CAPLUS

CN 1-Piperazineacetamide, N-[1-[[1-(aminoiminomethyl)-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-2-oxo-4-[(phenylmethyl)sulfonyl]- (9CI) (CA INDEX NAME)

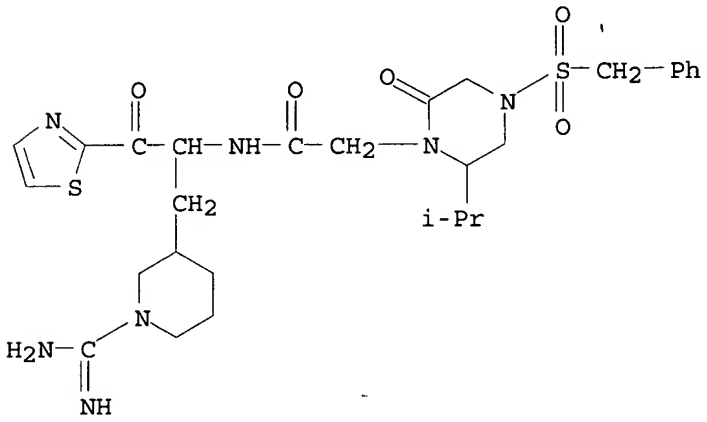


RN 204690-48-2 CAPLUS

CN 1-Piperazineacetamide, N-[1-[[1-(aminoiminomethyl)-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-2-oxo-6-(phenylmethyl)-4-[(phenylmethyl)sulfonyl]- (9CI) (CA INDEX NAME)

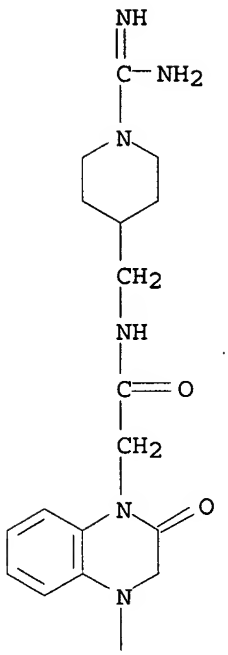


RN 204690-49-3 CAPLUS
CN 1-Piperazineacetamide, N-[1-[[1-(aminoiminomethyl)-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-2-(1-methylethyl)-6-oxo-4-[(phenylmethyl)sulfonyl]- (9CI) (CA INDEX NAME)

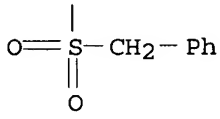


RN 204691-55-4 CAPLUS
CN 1(2H)-Quinoxalineacetamide, N-[[1-(aminoiminomethyl)-4-piperidinyl]methyl]-3,4-dihydro-2-oxo-4-[(phenylmethyl)sulfonyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



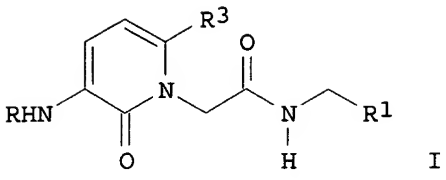
PAGE 2-A



L19 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1997:613883 CAPLUS
DN 127:293131
TI Preparation of 3-aralkylsulfonamido-2-oxodihydropyridine-1-acetamides and analogs as thrombin inhibitors
IN Sanderson, Philip E.; Naylor-Olsen, Adel M.; Dyer, Dona L.; Vacca, Joseph P.; Isaacs, Richard C. A.; Dorsey, Bruce D.; Fraley, Mark E.
PA Merck and Co., Inc., USA
SO U.S., 36 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5668289	A	19970916	US 1996-669189	19960624
	US 5744486	A	19980428	US 1997-829406	19970331
PRAI	US 1996-669189		19960624		

OS MARPAT 127:293131
GI



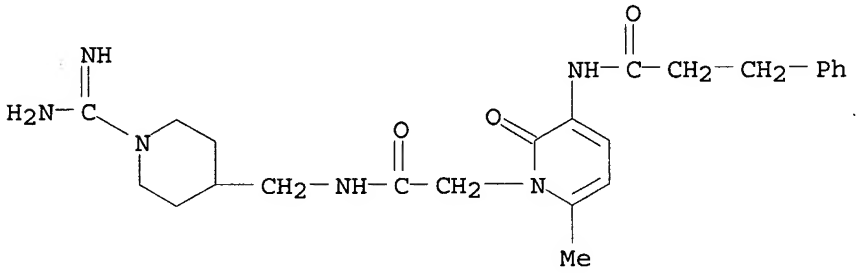
I

AB Title compds. [I; R = (phenyl)alkyl, alkoxycarbonyl, (un)substituted PhCH2SO2, etc.; R1 = trans-4-aminocyclohexyl, (un)substituted 6-amino-3-pyridinyl, etc.; R3 = H, (cyclo)alkyl, CF3] were prepd. Thus, 2-hydroxy-6-methylpyridine-3-carboxylic acid was refluxed with (PhO)2P(O)N3 and PhCH2OH and the product N-alkylated with BrCH2CO2CMe3 to give, in 3 addnl. steps, 3-benzylsulfonylamino-6-methyl-2-oxodihydropyridine-1-acetic acid which was amidated by trans-4-tert-butoxycarbonylaminocyclohexylmethylamine to give, after deprotection, I (R = PhCH2SO2, R1 = trans-4-aminocyclohexyl, R3 = Me). Data for biol. activity of I were given.

IT **187162-47-6P 187162-49-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3-aralkylsulfonamido-2-oxodihydropyridine-1-acetamides and analogs as thrombin inhibitors)

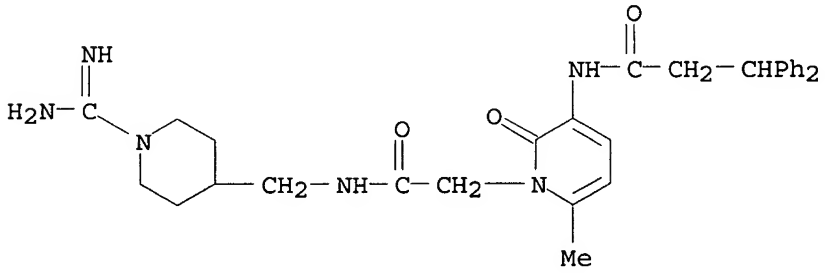
RN 187162-47-6 CAPLUS

CN 1(2H)-Pyridineacetamide, N-[[1-(aminoiminomethyl)-4-piperidinyl]methyl]-6-methyl-2-oxo-3-[(1-oxo-3-phenylpropyl)amino]- (9CI) (CA INDEX NAME)



RN 187162-49-8 CAPLUS

CN 1(2H)-Pyridineacetamide, N-[[1-(aminoiminomethyl)-4-piperidinyl]methyl]-6-methyl-2-oxo-3-[(1-oxo-3,3-diphenylpropyl)amino]- (9CI) (CA INDEX NAME)



L19 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2003 ACS

AN 1997:423742 CAPLUS

DN 127:136061

TI L-373,890, an achiral, noncovalent, subnanomolar thrombin inhibitor

AU Sanderson, Philip E. J.; Dyer, Dona L.; Naylor-Olsen, Adel M.; Vacca, Joseph P.; Gardell, Steven J.; Lewis, S. Dale; Lucas, Bobby J., Jr.; Lyle, Elizabeth A.; Lynch, Joseph J., Jr.; Mulichak, Anne M.

CS Merck Research Laboratories, Department of Medicinal Chemistry, West Point, PA, 19486, USA

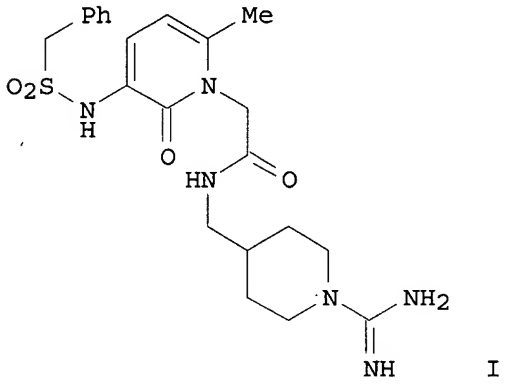
SO Bioorganic & Medicinal Chemistry Letters (1997), 7(12), 1497-1500
CODEN: BMCLE8; ISSN: 0960-894X

PB Elsevier

DT Journal

LA English

GI



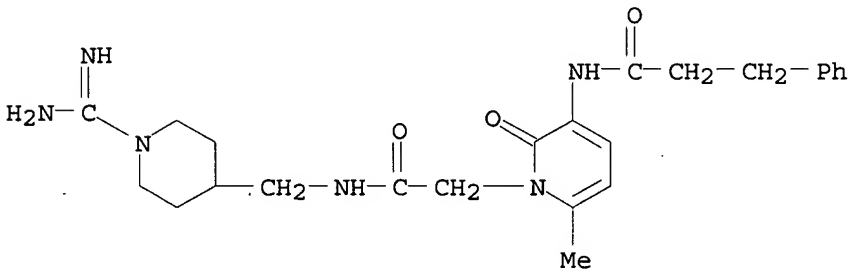
I

AB L-373,890 (I), a highly selective and efficacious pyridinone acetamide thrombin inhibitor was designed using a combination of X-ray crystallog., mol. modeling and empirical structure optimization.

IT **187162-47-6P 187162-49-8P 193151-01-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of pyridinone-based peptidomimetics as thrombin inhibitors)

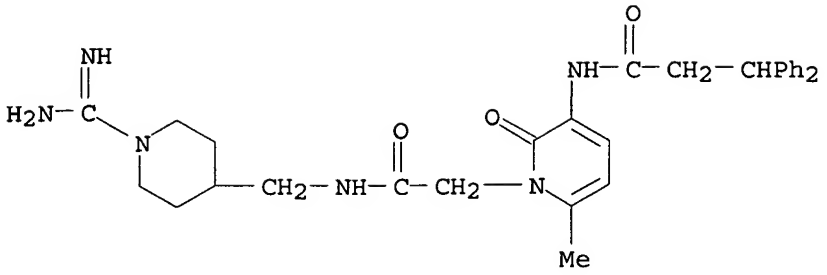
RN 187162-47-6 CAPLUS

CN 1(2H)-Pyridineacetamide, N-[[1-(aminoiminomethyl)-4-piperidinyl]methyl]-6-methyl-2-oxo-3-[(1-oxo-3-phenylpropyl)amino]- (9CI) (CA INDEX NAME)

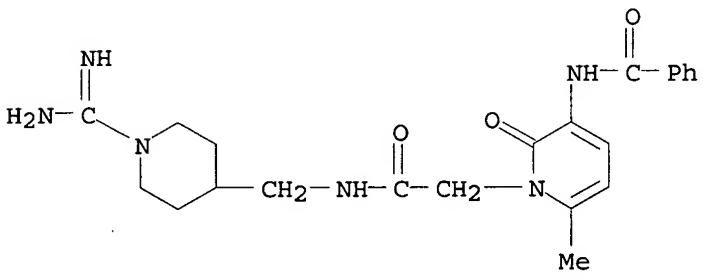


RN 187162-49-8 CAPLUS

CN 1(2H)-Pyridineacetamide, N-[[1-(aminoiminomethyl)-4-piperidinyl]methyl]-6-methyl-2-oxo-3-[(1-oxo-3,3-diphenylpropyl)amino]- (9CI) (CA INDEX NAME)



RN 193151-01-8 CAPLUS
CN 1(2H)-Pyridineacetamide, N-[[1-(aminoiminomethyl)-4-piperidinyl]methyl]-3-(benzoylamino)-6-methyl-2-oxo- (9CI) (CA INDEX NAME)



L19 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1997:178881 CAPLUS
DN 126:171490
TI Preparation of 2-pyridinones as thrombin inhibitors
IN Sanderson, Philip E.; Naylor-Olsen, Adel M.; Dyer, Dona L.; Vacca, Joseph P.; Isaacs, Richard C. A.; Dorsey, Bruce D.; Fraley, Mark E.
PA Merck and Co., Inc., USA; Sanderson, Philip E.; Naylor-Olsen, Adel M.; Dyer, Dona L.; Vacca, Josep, P.; Isaacs, Richard C. A.; Dorsey, Bruce D.; Fraley, Mark, E.
SO PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9701338	A1	19970116	WO 1996-US10778	19960624
	W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2224437	AA	19970116	CA 1996-2224437	19960624
	AU 9663917	A1	19970130	AU 1996-63917	19960624
	AU 703744	B2	19990401		
	EP 835109	A1	19980415	EP 1996-923399	19960624
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	JP 11508558	T2	19990727	JP 1996-504499	19960624
PRAI	US 1995-560P	P	19950627		
	US 1995-3818P	P	19950915		
	GB 1996-3450	A	19960219		

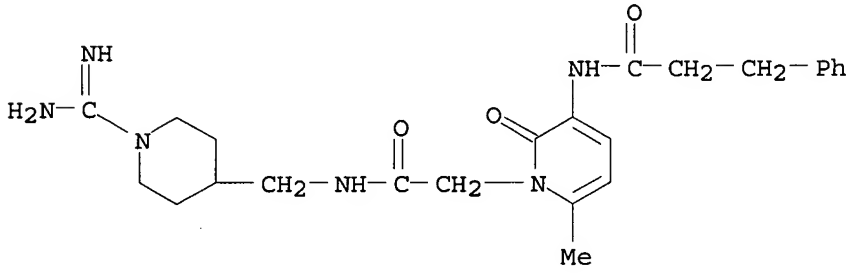
WO 1996-US10778 W 19960624
OS MARPAT 126:171490
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

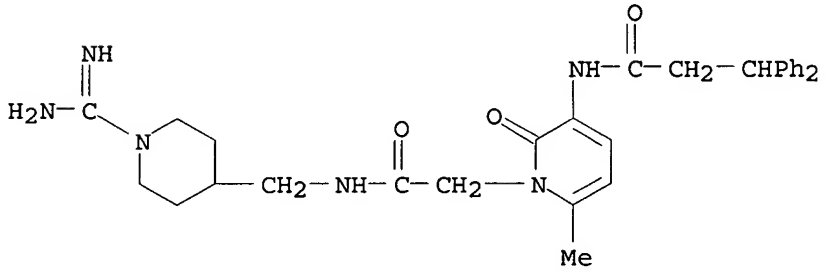
AB The title compds. [I; W = benzenemethylsulfonyl, diphenylmethylsulfonyl, naphthylsulfonyl, etc.; A = trans-4-aminocyclohexyl, 2-aminopyridin-4-yl, etc.; R3 = H, C1-4 alkyl, C3-7 cycloalkyl, CF3], useful in inhibiting thrombin and assocd. thrombotic occlusions, were prepd. Thus, reaction of PhCH2SO2Cl with 2-pyridinone II in the presence of Et3N in CH2Cl2 followed by treatment of the intermediate III in CH2Cl2/EtOAc with HCl gas, reaction of the Boc-deprotected intermediate with H2NC(:NH)SO3H in the presence of Et3N in DMF, and treatment of the resulting 2-pyridinone IV in MeOH/THF with 1M LiOH afforded V which showed Ki < 100 nM against human thrombin and Ki of > 500 nM against human trypsin.

IT **187162-47-6P 187162-49-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2-pyridinones as thrombin inhibitors)

RN 187162-47-6 CAPLUS
CN 1(2H)-Pyridineacetamide, N-[[1-(aminoiminomethyl)-4-piperidinyl]methyl]-6-methyl-2-oxo-3-[(1-oxo-3-phenylpropyl)amino]- (9CI) (CA INDEX NAME)



RN 187162-49-8 CAPLUS
CN 1(2H)-Pyridineacetamide, N-[[1-(aminoiminomethyl)-4-piperidinyl]methyl]-6-methyl-2-oxo-3-[(1-oxo-3,3-diphenylpropyl)amino]- (9CI) (CA INDEX NAME)



L19 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1996:222238 CAPLUS
DN 124:290275
TI Preparation of peptide aldehydes containing 3-amino-2-oxo-1-

piperidineacetic derivative and an arginine mimic as specific inhibitors of thrombin

IN Semple, Joseph E.; Levy, Odile E.; Nutt, Ruth F.; Ripka, William C.

PA Corvas International, Inc., USA

SO PCT Int. Appl., 114 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9535313	A1	19951228	WO 1995-US7832	19950619
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5714499	A	19980203	US 1994-261498	19940617
	US 5932733	A	19990803	US 1995-482117	19950607
	AU 9529054	A1	19960115	AU 1995-29054	19950619
	EP 765339	A1	19970402	EP 1995-924623	19950619
	EP 765339	B1	19990127		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 10503177	T2	19980324	JP 1995-502570	19950619
PRAI	US 1994-261498		19940617		
	US 1994-356831		19941213		
	US 1995-482117		19950607		
	WO 1995-US7832		19950619		

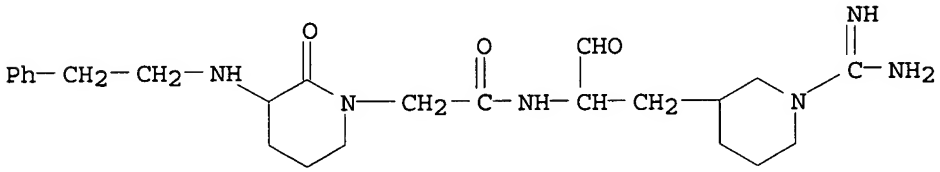
OS MARPAT 124:290275

GI For diagram(s), see printed CA Issue.

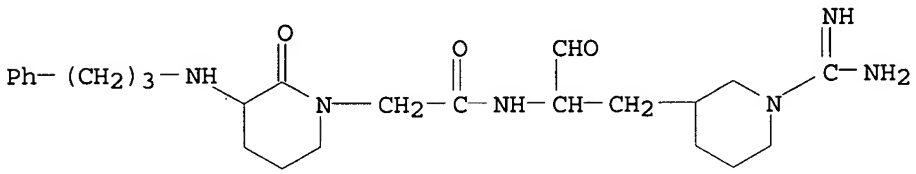
AB The title peptide aldehydes [I; X = SO2, NR'SO2, CO, O2C, NHCO, P(O)R'', direct link; wherein R' = H, C1-4 alkyl, C6-14 aryl, C6-16 aralkyl; R'' = NR', OR', SR', provided that R'' .noteq. NH, OH, H, or SH; R1 = C1-12 alkyl, (un)substituted C5-8 cycloalkyl-C1-3 alkyl, (un)substituted C3-15 cycloalkyl, (un)substituted C4-10 heterocycloalkyl, C4-10 heterocyclyl, or C5-14 heteroaryl contg. heteroatoms selected from O, N, S, SO, and SO2, (un)substituted C3-6 alkenyl, (un)substituted C6-14 aryl, (un)substituted aralkyl, Q1, etc., provided that Y .noteq. Q1; wherein Q1 = 5- to 7-membered heterocycle of 3-6 ring C atoms; V = CH2, O, S, SO, SO2; Q = (CH2)n, (CH2)qR4; wherein n = 1-4; q = 1,2; R4 = S, SO, SO2, O, (un)substituted NH; R2 = H, C1-4 alkyl, C2-4 alkenyl; Y = group selected from R1, provided that Y .noteq. Q1; R3 = Q2, Q3; wherein W = N, CH] and their pharmaceutically acceptable salts, which are potent and specific inhibitors of thrombin and are useful as therapeutic agents (e.g. antithrombotic agents) for disease states in mammals characterized by abnormal thrombosis, are prepd. Thus, (S)-3-(benzylsulfonylamino)hexahydro-2-oxo-1-piperidineacetic acid (prepn. given) was condensed with 3-(3-piperidyl)-L-alaninol deriv. (II) using 1-hydroxybenzotriazole monohydrate, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, 4-dimethylaminopyridine, and Et3N in MeCN to give the dipeptide intermediate (III; R = CH2OH, R5 = CO2CH2Ph). The latter compd. was hydrogenated in the presence of 10% Pd-C in AcOH/MeOH at 45 psi for 3 h to give III.AcOH (R = CH2OH, R5 = H), which was oxidized by DMSO, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, and dichloroacetic acid at 0.degree. for 5 min and at ambient temp. for 85 min to give, after purifn. by reverse phase HPLC, two diastereomers of the title dipeptide III (R = CHO, R5 = H). The slower-moving diastereomer in HPLC in vitro showed IC50 of 0.8 nM against human .alpha.-thrombin and did not inhibit serine proteases such as recombinant tissue plasminogen activator, plasmin, activated protein C, chymotrypsin, and trypsin at 2,5000 nM.

IT **175281-98-8P 175281-99-9P 175282-00-5P**
175282-01-6P 175282-02-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptide aldehydes contg. aminooxopiperidineacetic deriv. and arginine mimic as specific thrombin inhibitors and antithrombotics)

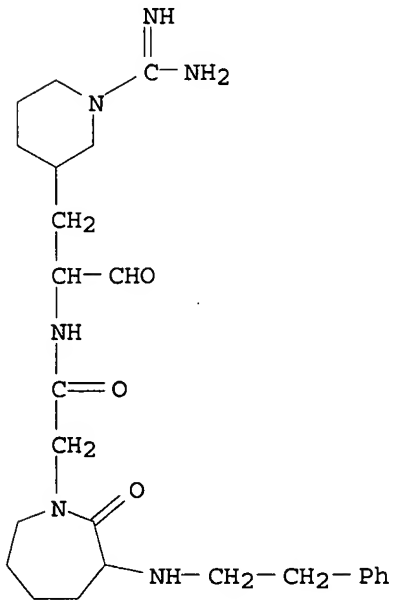
RN 175281-98-8 CAPLUS
CN 1-Piperidineacetamide, N-[2-[1-(aminoiminomethyl)-3-piperidinyl]-1-formylethyl]-2-oxo-3-[(2-phenylethyl)amino]- (9CI) (CA INDEX NAME)



RN 175281-99-9 CAPLUS
CN 1-Piperidineacetamide, N-[2-[1-(aminoiminomethyl)-3-piperidinyl]-1-formylethyl]-2-oxo-3-[(3-phenylpropyl)amino]- (9CI) (CA INDEX NAME)

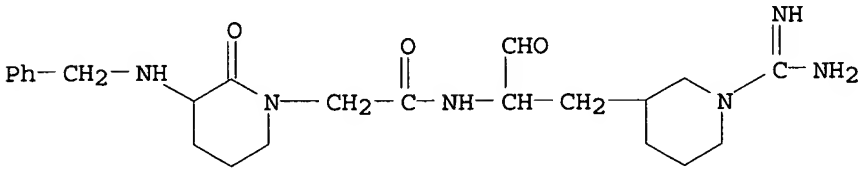


RN 175282-00-5 CAPLUS
CN 1H-Azepine-1-acetamide, N-[2-[1-(aminoiminomethyl)-3-piperidinyl]-1-formylethyl]hexahydro-2-oxo-3-[(2-phenylethyl)amino]- (9CI) (CA INDEX NAME)



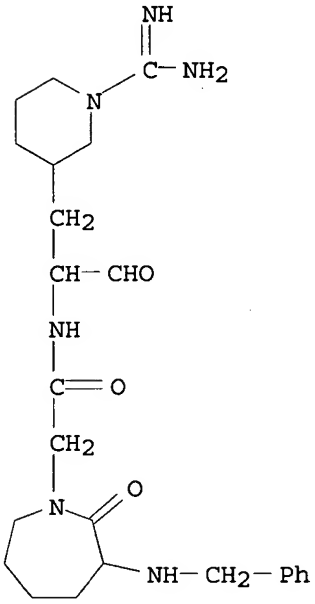
RN 175282-01-6 CAPLUS

CN 1-Piperidineacetamide, N-[2-[1-(aminoiminomethyl)-3-piperidinyl]-1-formylethyl]-2-oxo-3-[(phenylmethyl)amino]- (9CI) (CA INDEX NAME)

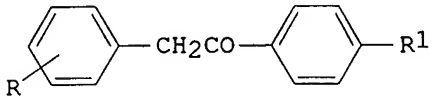


RN 175282-02-7 CAPLUS

CN 1H-Azepine-1-acetamide, N-[2-[1-(aminoiminomethyl)-3-piperidinyl]-1-formylethyl]hexahydro-2-oxo-3-[(phenylmethyl)amino]- (9CI) (CA INDEX NAME)



AN 1977:89337 CAPLUS
DN 86:89337
TI Synthesis of amidinobenzylaryl-, amidinobenzylalkyl-, and amidinobenzylalkoxymethyl ketones
AU Wagner, G.; Voigt, B.; Schramm, C.
CS Sekt. Biowiss., Karl-Marx-Univ., Leipzig, Ger. Dem. Rep.
SO Pharmazie (1976), 31(7), 432-6
CODEN: PHARAT; ISSN: 0031-7144
DT Journal
LA German
GI



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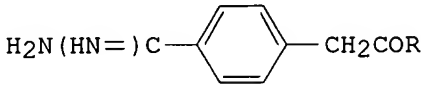
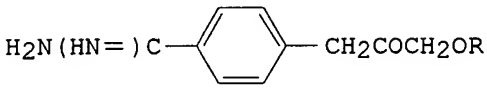
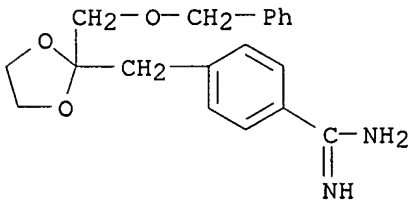


II



III

AB The title compds. [I; R = 3-C(:NH)NH2, 4-C(:NH)NH2; R1 = H, Cl, OH, Me, MeO, Ph, PhO; II; R = Me, Pr, PhCH2; III; R = Et, PhCH2] are prepd. by std. procedures. Thus, reaction of 4-NCC6H4CH2COCl with PhOH in CS2 in presence of AlCl3 gives 38% 4-NCC6H4CH2COC6H4OH-4 which reacts with MeOH in dioxane in presence of HCl to give 50% 4-[MeO(HN:)C]C6H4CH2COC6H4OH-4 (IV). Reaction of IV with NH3 in EtOH gives 75% I.HCl [R = 4-C(:NH)NH2].
IT **62044-34-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and hydrolysis of)
RN 62044-34-2 CAPLUS
CN Benzenecarboximidamide, 4-[[2-[(phenylmethoxy)methyl]-1,3-dioxolan-2-yl]methyl]-, monohydrochloride (9CI) (CA INDEX NAME)

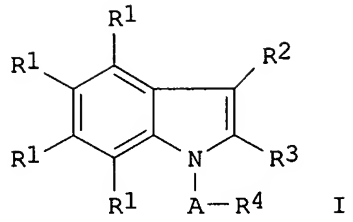


● HCl

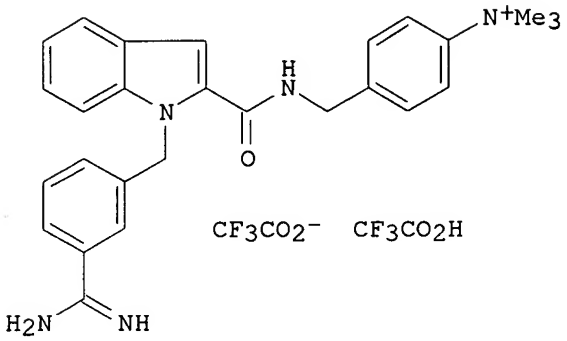
AN 1999:460399 CAPLUS
DN 131:87814
TI Indole derivatives as inhibitors of factor Xa, and their preparation and use as anticoagulants
IN Defossa, Elisabeth; Heinelt, Uwe; Klingler, Otmar; Zoller, Gerhard; Al-Obeidi, Fahad; Walser, Armin; Wildgoose, Peter; Matter, Hans
PA Hoechst Marion Roussel Deutschland Gmbh, Germany
SO PCT Int. Appl., 199 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9933800	A1	19990708	WO 1998-EP8030	19981210
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2316172	AA	19990708	CA 1998-2316172	19981210
	AU 9920528	A1	19990719	AU 1999-20528	19981210
	AU 743881	B2	20020207		
	BR 9814340	A	20001003	BR 1998-14340	19981210
	EP 1042287	A1	20001011	EP 1998-965244	19981210
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI				
	JP 2001527066	T2	20011225	JP 2000-526484	19981210
	NZ 505370	A	20020628	NZ 1998-505370	19981210
	ZA 9811759	A	19990728	ZA 1998-11759	19981222
	NO 2000003057	A	20000818	NO 2000-3057	20000614
	US 6337344	B1	20020108	US 2000-582344	20000814
PRAI	EP 1997-122901	A	19971224		
	WO 1998-EP8030	W	19981210		

OS MARPAT 131:87814
GI



I



II

AB The invention relates to the inhibition of blood clotting proteins, and more particularly, to indole derivs. or their physiol. acceptable salts which effect this, having formula I [R1 groups = H, halo, alkyl, CF3, (un)substituted Ph or phenylalkoxy, etc., with .gtoreq.2 of R1 being H; .gtoreq.1 of R2 and R3 = (CH2)0-2CO2H or derivs., other = H, F, Cl, Br, or alkyl; or R2R3 = CH2CH2N(COPh)CH2 or analogs; A = bond, alk(en/yn)ylene, CO, SO, SO2, etc.; R4 = (un)substituted Ph, pyridyl, or other heterocyclyl]. I are inhibitors of the blood clotting enzyme factor Xa. The invention also relates to processes for the prepn. of I, to methods of inhibiting factor Xa activity and blood clotting, to use of I in the treatment and prophylaxis of assocd. (e.g., thromboembolic) diseases, and to the use of I in the prepn. of related medicaments. The invention further relates to compns. contg. I, in particular pharmaceutical compns. contg. a compd. I and pharmaceutically acceptable carriers and/or auxiliary substances. Over 160 compds. I were prepd. For instance, 1H-indole-2-carboxylic acid Et ester underwent a 5-step sequence to give title salt II. This prepn. involved (1) N-alkylation with 3-cyanobenzyl bromide, (2) alk. hydrolysis of the ester, (3) amidation with 4-(Me2N)C6H4CH2NH2.2HCl, (4) conversion of the nitrile to a thioamide, and (5) quaternization at dimethylamino, and ammonolysis of the thioamide to an amidine. In an assay using human factor Xa in vitro, II had a Ki value of 0.090 .mu.M.

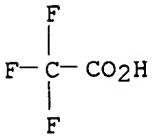
IT **229951-27-3P 229951-34-2P 229954-46-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(target compd.; prepn. of indole derivs. as inhibitors of factor Xa)

RN 229951-27-3 CAPLUS

CN Benzenaminium, .4-[[[[1-[[3-(aminoiminomethyl)phenyl]methyl]-5-(phenylmethoxy)-1H-indol-2-yl]carbonyl]amino]methyl]-N,N,N-trimethyl-, salt with trifluoroacetic acid (1:1), mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 76-05-1
CMF C2 H F3 O2

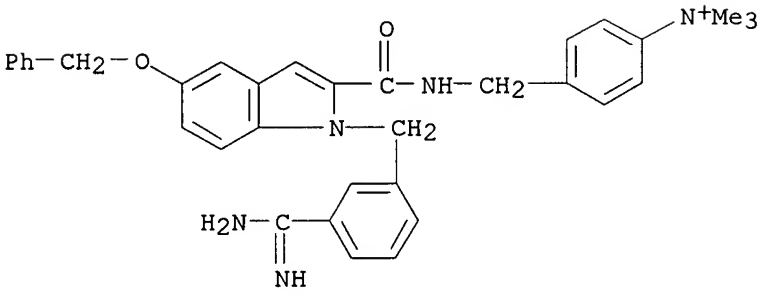


CM 2

CRN 229951-26-2
CMF C34 H36 N5 O2 . C2 F3 O2

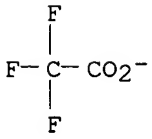
CM 3

CRN 229951-25-1
CMF C34 H36 N5 O2

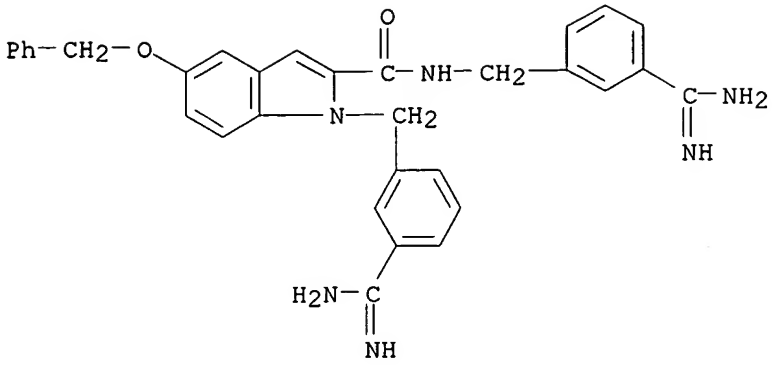


CM 4

CRN 14477-72-6
CMF C2 F3 O2



RN 229951-34-2 CAPLUS
CN 1H-Indole-2-carboxamide, N,1-bis[[3-(aminoiminomethyl)phenyl]methyl]-5-(phenylmethoxy)-, dihydriodide (9CI) (CA INDEX NAME)

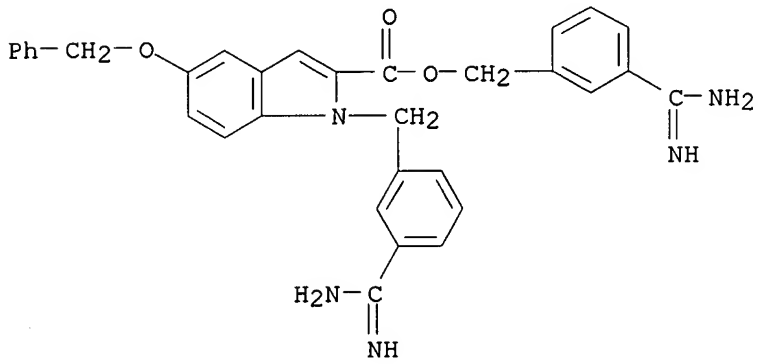


●2 HI

RN 229954-46-5 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[[3-(aminoiminomethyl)phenyl]methyl]-5-(phenylmethoxy)-, [3-(aminoiminomethyl)phenyl]methyl ester, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

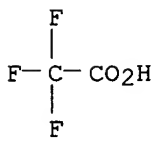
CM 1

CRN 229951-49-9
CMF C32 H29 N5 O3



CM 2

CRN 76-05-1
CMF C2 H F3 O2



IT **229950-49-6P 229951-50-2P 229951-52-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compd.; prepn. of indole derivs. as inhibitors of factor Xa)

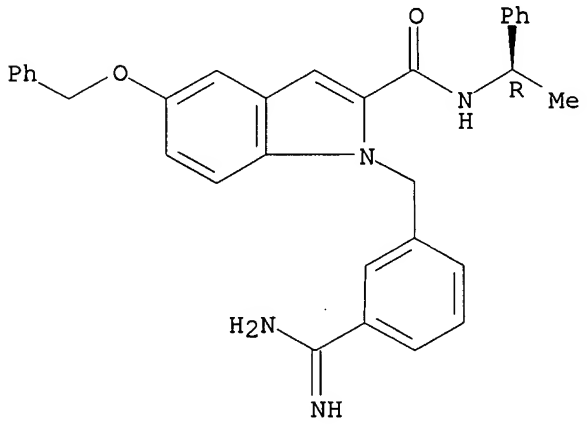
RN 229950-49-6 CAPLUS

CN 1H-Indole-2-carboxamide, 1-[[3-(aminoiminomethyl)phenyl]methyl]-N-[(1R)-1-phenylethyl]-5-(phenylmethoxy)-, monoacetate (9CI) (CA INDEX NAME)

CM 1

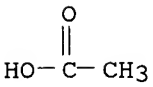
CRN 229950-48-5
CMF C32 H30 N4 O2

Absolute stereochemistry.



CM 2

CRN 64-19-7
CMF C2 H4 O2

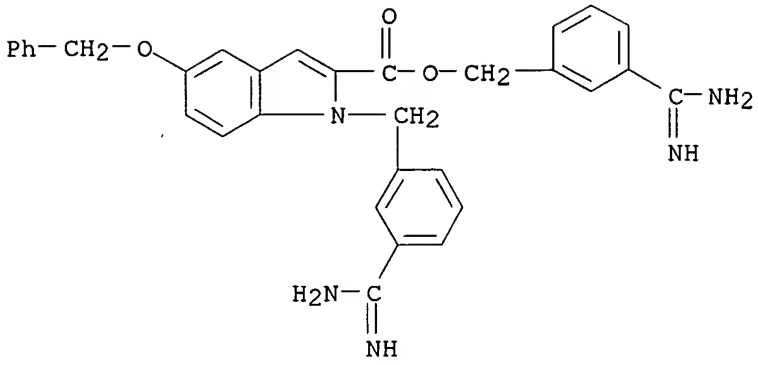


RN 229951-50-2 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[[3-(aminoiminomethyl)phenyl]methyl]-5-(phenylmethoxy)-, [3-(aminoiminomethyl)phenyl]methyl ester, diacetate (9CI) (CA INDEX NAME)

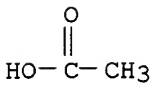
CM 1

CRN 229951-49-9
CMF C32 H29 N5 O3

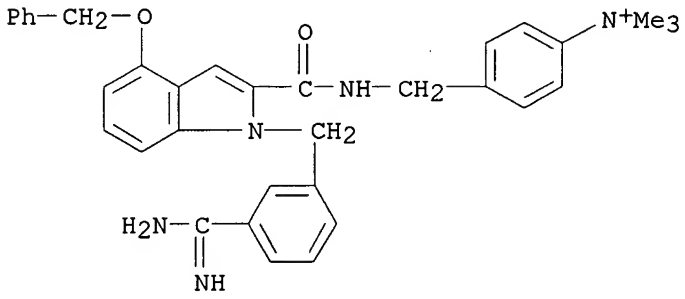


CM 2

CRN 64-19-7
CMF C2 H4 O2



RN 229951-52-4 CAPLUS
CN Benzenaminium, 4-[[[[1-[[3-(aminoiminomethyl)phenyl]methyl]-4-(phenylmethoxy)-1H-indol-2-yl]carbonyl]amino]methyl]-N,N,N-trimethyl-, iodide, monohydriodide (9CI) (CA INDEX NAME)



● I^-

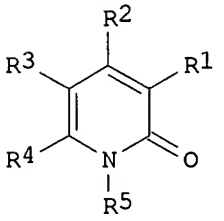
● HI

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

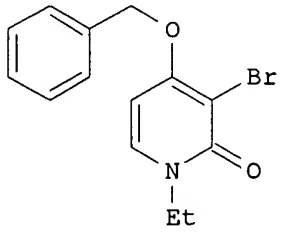
AN 2003:656582 CAPLUS
DN 139:197371
TI Preparation of substituted pyridinones as modulators of p38 MAP kinase
IN Devadas, Balekudru; Walker, John; Selness, Shaun R.; Boehm, Terri L.; Durley, Richard C.; Devraj, Rajesh; Hickory, Brian S.; Rucker, Paul V.; Jerome, Kevin D.; Madsen, Heather M.; Alvira, Edgardo; Promo, Michele A.; Blevis-Bal, Radhika M.; Marrufo, Laura D.; Hitchcock, Jeff; Owen, Thomas; Naing, Win; Xing, Li; Shieh, Huey S.; Sambandam, Aruna; Liu, Shuang; Scott, Ian L.; McGee, Kevin F.
PA Pharmacia Corporation, USA
SO PCT Int. Appl., 1052 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068230	A1	20030821	WO 2003-US4634	20030214

PI WO 2003068230 A1 20030821 WO 2003-US4634 20030214
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI US 2002-357029P P 20020214
US 2002-436915P P 20021230
OS MARPAT 139:197371
GI



I



II

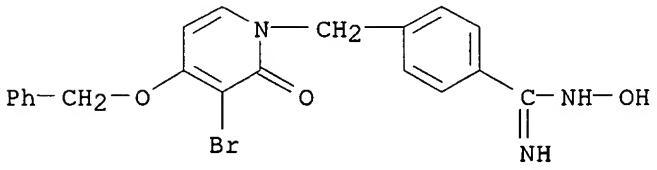
AB Disclosed are title compds. I [wherein R1 = H, halo, NO2, CHO, CN, CO2H, or (un)substituted (halo)alkyl, (aryl)alkoxy, aryl(alkyl), alkenyl, (aryl)alkynyl, (aryl)alkanoyl, alkoxyalkyl, or haloalkoxy; R2 = H, OH, halo, NR8R9, CO2R, or (un)substituted OSO2-alkyl, OSO2-aryl, arylalkoxy, aryloxy(alkyl), arylthio(alkoxy), arylalkynyl, alkoxy(alkoxy), alkyl, alkynyl, OCONH(CH2)n-aryl, OCON(alkyl)(CH2)n-aryl, dialkylamino, (hetero)aryl(alkyl), arylalkenyl, or heterocycloalkyl(alkyl); R3 = H, halo, alkenyl, NR6R7, NR6R7-alkyl, alkyl, or (un)substituted (aryl)alkoxycarbonyl, aryloxycarbonyl, arylalkyl, OCONH(CH2)n-aryl, arylalkoxy, OCON(alkyl)(CH2)n-aryl, aryloxy, arylthio, or (aryl)thioalkoxy; R4 = H or (un)substituted alkyl; R5 = H, aryl, aryl(thio)alkyl, NH2, alkoxycarbonyl, alkynyl, SO2-alkyl, (hetero)cycloalkyl(alkyl), heteroaryl, or (un)substituted alkyl, alkoxy(alkyl), or alkenyl; R6 and R7 = independently H, OH, or (un)substituted (aryl)alkyl, alkoxy(alkyl), alkanoyl(alkyl), arylalkoxy,

SO2-alkyl, (aryl)alkoxycarbonyl, heteroarylalkyl, or arylalkanoyl; or NR6R7 = (un)substituted (thio)morpholinyl, pyrrolidinyl, piperidinyl, pyrrolidinyl, or piperazinyl; R8 = independently H or (un)substituted (aryl)alkyl or (aryl)alkanoyl; R9 = H or (un)substituted (aryl)alkyl, (aryl)alkanoyl, cycloalkyl(alkyl), alkenyl, heteroaryl, (alkyl)aminoalkyl, SO2Ph, or aryl; R = independently H or (un)substituted alkyl; n = 0-6; and pharmaceutically acceptable salts thereof]. These compds. are useful for treating diseases and conditions caused or exacerbated by unregulated p38 MAP Kinase and/or TNF activity, such as inflammation, ischemia, viral infections, and autoimmune diseases (no data). Pharmaceutical compns. contg. I, methods of prepg. them, and methods of treatment using the compds. are also disclosed. For example, reaction of 4-benzyloxy-2(1H)-pyridone with EtBr in the presence of K2CO3 in DMF gave II. The latter inhibited MKK6-activated human p38.alpha. kinase phosphorylation of a biotinylated substrate or human p38.alpha.-induced phosphorylation of EGFRP (epidermal growth factor receptor peptide) with an IC50 in the range of 1 .mu.M to 25 .mu.M.

IT **586372-89-6P**, 4-[[4-(Benzyloxy)-3-bromo-2-oxo-2H-pyridin-1-yl]methyl]-N'-hydroxybenzenecarboximidamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(p38 kinase inhibitor; prepn. of pyridinones as modulators of p38 MAP kinase for treatment of inflammatory conditions, ischemia, viral infections, autoimmune diseases, and other conditions)

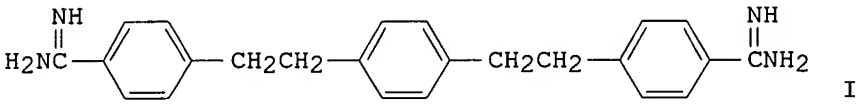
RN 586372-89-6 CAPLUS

CN Benzenecarboximidamide, 4-[[3-bromo-2-oxo-4-(phenylmethoxy)-1(2H)-pyridinyl]methyl]-N-hydroxy- (9CI) (CA INDEX NAME)

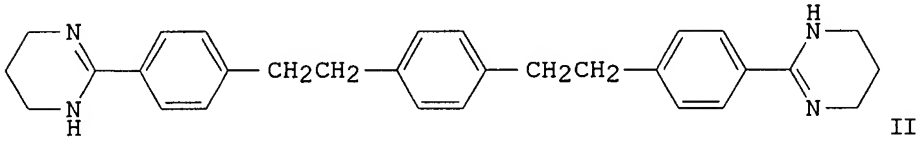


RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN 1982:400333 CAPLUS
DN 97:333
TI 1,4-Bis(4-guanylphenylethyl)benzenes as potential antitrypanosomal agents
AU Das, Bijan P.; Zalkow, Vera B.; Forrester, Margret L.; Molock, Frank F.; Boykin, David W.
CS Dep. Chem., Georgia State Univ., Atlanta, GA, 30303, USA
SO Journal of Pharmaceutical Sciences (1982), 71(4), 465-6
CODEN: JPMSAE; ISSN: 0022-3549
DT Journal
LA English
OS CASREACT 97:333
GI



I

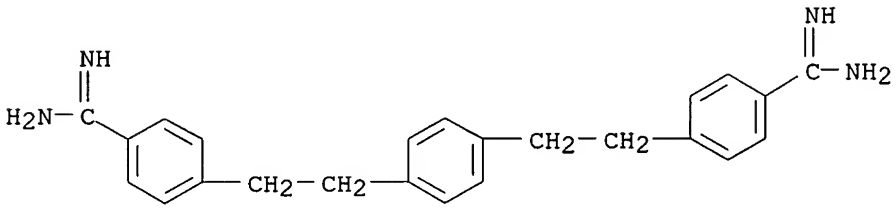


II

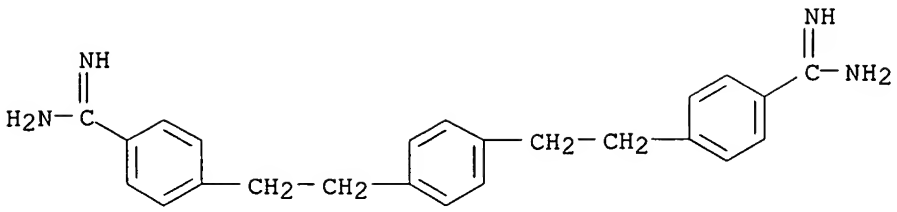
AB Five 1,4-bis(4-guanylphenylethyl)benzenes, including masked amidines in which the guanyl function is incorporated into a heterocyclic ring, were prepd. for screening as potential antitrypanosomal agents. Some of these compds. were active against Trypanosoma rhodesiense in mice. The diamidines were prepd. by std. methods from 1,4-bis(4-cyanophenylethyl)benzene [81919-21-3] which was obtained from 1,4-bis(4-cyanostyryl)benzene [13001-40-6] by diimide redn. The bis guanyl compd. I [**81919-15-5**] had good activity providing cures down to dosage of 26 mg/kg. The 2 masked amidines showed different activities in the screen; II [81919-16-6] while toxic at high doses, was slightly more active than I at low doses.

IT **81919-15-5DP**, derivs. **81919-15-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and antitrypanosomal activity of)

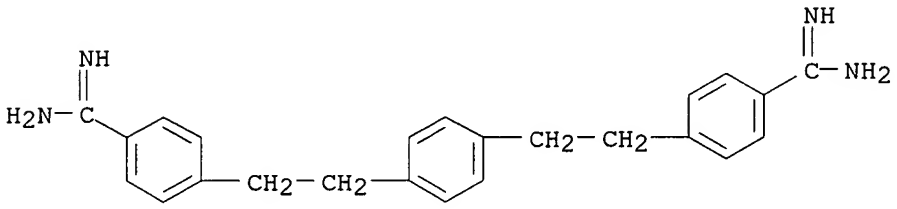
RN 81919-15-5 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-phenylenedi-2,1-ethanediyl)bis- (9CI) (CA INDEX NAME)



RN 81919-15-5 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-phenylenedi-2,1-ethanediyl)bis- (9CI) (CA INDEX NAME)



IT **81919-22-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 81919-22-4 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-phenylenedi-2,1-ethanediyl)bis-, dihydrochloride (9CI) (CA INDEX NAME)

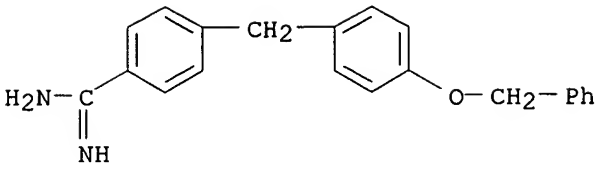


● 2 HCl

AN 1998:180759 CAPLUS
DN 128:243953
TI Preparation of N-aralkylpyridine-4-amines and analogs as thrombin inhibitors
IN Naylor-Olsen, Adel M.; Ponticello, Gerald S.; Vacca, Joseph P.; Hungate, Randall W.; Coburn, Craig; Phillips, Brian T.; Lewis, S. D.; Fraley, Mark E.
PA Merck & Co., Inc., USA; Naylor-Olsen, Adel M.; Ponticello, Gerald S.; Vacca, Joseph P.; Hungate, Randall W.; Coburn, Craig; Phillips, Brian T.; Lewis, S. D.; Fraley, Mark E.
SO PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

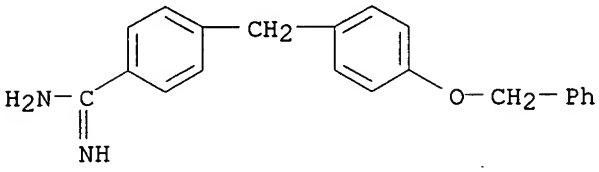
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9810763	A1	19980319	WO 1997-US15989	19970909
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9744117	A1	19980402	AU 1997-44117	19970909
	AU 725403	B2	20001012		
	EP 927035	A1	19990707	EP 1997-942415	19970909
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	JP 2001500864	T2	20010123	JP 1998-513809	19970909
PRAI	US 1996-26033P	P	19960913		
	GB 1996-24278	A	19961122		
	WO 1997-US15989	W	19970909		

OS MARPAT 128:243953
AB R1CHR2Z1Z2Z3R [I; R = 4-pyridyl, 4-amidino-1-piperazinyl, 4-aminopyridinium-1-yl, 6-amino- or amidino-3-pyridyl, C6H4[C(:NH)NH2]-4; R1,R2 = H, (hetero)aryl, (di)arylalkyl, CONH2, etc.; R1R2 = alkylene; Z1 = O, SO0-2, (alkyl)imino, etc.; Z2 = (un)substituted phenylene; Z3 = (CH2)m, (CH2)mNH, SO2NH, SO2(CH2)m, SO2, (CH2)mSO2; m = 1 or 2] were prepd. Thus, 4-(PhO)C6H4CO2H was amidated by 4-aminopyridine and the product reduced to give 4-(PhO)C6H4CH2NHR (R = 4-pyridyl). Data for biol. activity of I were given.
IT **204840-19-7P 204840-23-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-aralkylpyridine-4-amines and analogs as thrombin inhibitors)
RN 204840-19-7 CAPLUS
CN Benzenecarboximidamide, 4-[[4-(phenylmethoxy)phenyl]methyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 204840-23-3 CAPLUS
CN Benzenecarboximidamide, 4-[[4-(phenylmethoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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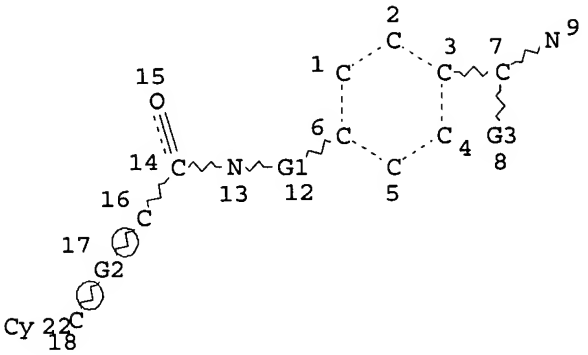
L8 HAS NO ANSWERS
L8 STR



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VAR G3=C/N
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 6
NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE

=> s l8 ful
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FULL SCREEN SEARCH COMPLETED - 5187 TO ITERATE

100.0% PROCESSED 5187 ITERATIONS 147 ANSWERS
SEARCH TIME: 00.00.01

L10 147 SEA SSS FUL L8

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	447.65	447.86

FILE 'CAPLUS' ENTERED AT 16:45:39 ON 14 APR 2003
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FILE COVERS 1907 - 14 Apr 2003 VOL 138 ISS 16

FILE LAST UPDATED: 13 Apr 2003 (20030413/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l10
L11 8 L10

=> d bib abs 1-8

L11 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 2002:170736 CAPLUS
DN 137:63452
TI Synthesis of Potential Thrombin Inhibitors. Incorporation of Tartaric Acid Templates as P2 Proline Mimetics
AU Dahlgren, Anders; Branalt, Jonas; Kvarnstrom, Ingemar; Nilsson, Ingemar; Musil, Djordje; Samuelsson, Bertil
CS Department of Chemistry, Linkoping University, Linkoping, S-581 83, Swed.
SO Bioorganic & Medicinal Chemistry (2002), 10(5), 1567-1580
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 137:63452
AB With the objective to prep. novel non-peptidic thrombin inhibitors, bioisosteres of the inhibitory tripeptide D-Phe-Pro-Arg chain have been examd. Thus, the P1 Arg was replaced with p-amidinobenzylamine, an elongated homolog of the same and with 2,5-dichloro benzylamine. The P2-P3, D-Phe-Pro, was replaced with a novel tartaric acid template coupled to a series of readily available, mainly lipophilic, amines. Some of these compds. exhibit promising thrombin inhibition activity in vitro, IC50.apprx.5.9 .mu.M.
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

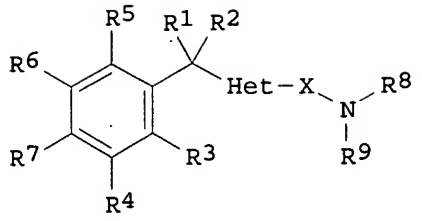
L11 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 2001:150305 CAPLUS
DN 135:15886
TI Computational modelling of inhibitor binding to human thrombin
AU Ljungberg, K. B.; Marelius, J.; Musil, D.; Svensson, P.; Norden, B.; Aqvist, J.
CS BMC, Department of Cell and Molecular Biology, Uppsala University, Uppsala, SE-751 24, Swed.
SO European Journal of Pharmaceutical Sciences (2001), 12(4), 441-446
CODEN: EPSCED; ISSN: 0928-0987
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
AB Thrombin is an essential protein involved in blood clot formation and an important clin. target, since disturbances of the coagulation process cause serious cardiovascular diseases such as thrombosis. Here the authors evaluate the performance of a mol. dynamics based method for predicting the binding affinities of different types of human thrombin inhibitors. For a series of eight ligands, the method ranks their relative affinities reasonably well. The binding free energy difference between high and low affinity representatives in the test set is quant. reproduced, as well as the stereospecificity for a chiral inhibitor. The original parametrization of this linear interaction energy method requires the addn. of a const. energy term in the case of thrombin. This yields a mean unsigned error of 0.68 kcal/mol for the abs. binding free energies. This type of approach is also useful for elucidating three-dimensional structure-activity relationships in terms of microscopic interactions of

the ligands with the solvated enzyme.
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 2000:241135 CAPLUS
DN 132:279106
TI Non-peptide GnRH agents, methods and intermediates for their preparation
IN Anderson, Mark Brian; Vazir, Haresh N.; Luthin, David Robert; Paderes, Genevieve Deguzman; Pathak, Ved P.; Christie, Lance Christopher; Hong, Yufeng; Tompkins, Eileen Valenzuela; Li, Haitao; Faust, James
PA Agouron Pharmaceuticals, Inc., USA; et al.
SO PCT Int. Appl., 444 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000020358	A2	20000413	WO 1999-US18790	19990820
	WO 2000020358	A3	20001116		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2341346	AA	20000413	CA 1999-2341346	19990820
	BR 9913374	A	20010515	BR 1999-13374	19990820
	EP 1105120	A2	20010613	EP 1999-968010	19990820
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	EE 200100102	A	20020617	EE 2001-20010010219990820	
	JP 2002535244	T2	20021022	JP 2000-574479	19990820
	NO 2001000309	A	20010411	NO 2001-309	20010119
	LV 12732	B	20020320	LV 2001-45	20010316
	LT 4904	B	20020425	LT 2001-24	20010319
PRAI	US 1998-97520P	P	19980820		
	WO 1999-US18790	W	19990820		

OS MARPAT 132:279106
GI



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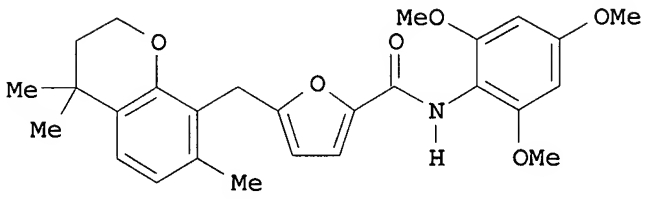


II

AB Non-peptide GnRH agents capable of inhibiting the effect of gonadotropin-releasing hormone are described. The compds. and their pharmaceutically acceptable salts, multimers, prodrugs, and active metabolites are suitable for treating mammalian reproductive disorders and steroid hormone-dependent tumors as well as for regulating fertility, where suppression of gonadotropin release is indicated. The compds. include those of formula I [X = C:O, C:S, S:O, or SO2; Het = 5-membered NOS-heterocycle; R1, R2 = H, alkyl; R3-R7 = H, halo, (un)substituted alkyl, aryl, heteroaryl, CH2OR, OR, CO2R; R = alkyl, aryl, etc.; adjacent rings positions such as R6R7 may form (un)substituted 5- or 6-membered ring with up to 4 heteroatoms; R8 = lipophilic moiety such as alkyl, aryl, CH2OR, OR, etc.; R9 = H, (un)substituted alkyl]. Methods and intermediates for synthesizing the compds. are also described. For instance, 4,4,7-trimethylchroman (prepn. given) was alkylated in the 6- and 8-positions using Et 5-(chloromethyl)-2-furoate (46% total yield), and the resulting esters were hydrolyzed to a mixt. of acids. This unsepd. mixt. was treated with SOCl2 and amidated with 2,4,6-trimethoxyphenylamine-HCl to give the invention compd. II and its chroman-6-position isomer, which were sepd. by HPLC. Several compds. exhibited high affinity (<100 nM) at human GnRH receptors. The compds. antagonized GnRH-stimulated inositol phosphate accumulation in cells with recombinant human GnRH receptors, and an example compd. reduced plasma LH levels in castrated male rats. Various biol. data for several hundred compds. are given.

L11 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 1999:529128 CAPLUS
DN 131:184864
TI Preparation of amidinophenylcarbamoylbiphenyl derivatives and heterocyclic analogs thereof as inhibitors of blood coagulation factor VIIa
IN Senokuchi, Kazuhiko; Ogawa, Koji
PA Ono Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 665 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

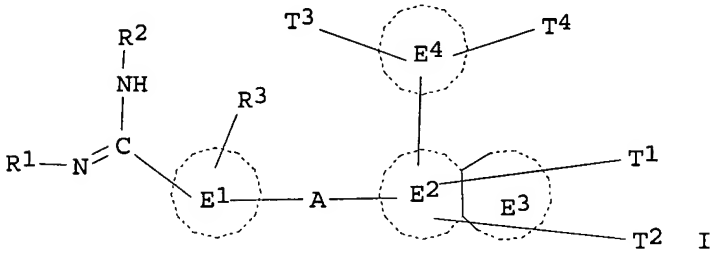
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9941231	A1	19990819	WO 1999-JP622	19990212

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG,

KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	AU 9923006	A1	19990830	AU 1999-23006	19990212
	EP 1078917	A1	20010228	EP 1999-902896	19990212
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	ZA 9901273	A	19990825	ZA 1999-1273	19990217
	US 6358960	B1	20020319	US 2000-601998	20000811
PRAI	JP 1998-76815	A	19980217		
	WO 1999-JP622	W	19990212		

OS MARPAT 131:184864
GI



I

AB The title compds. I [T1 = (R5)q; T2 = (R7)n; T3 = (R6)m; T4 = (R4)p; R1, R2 = H, alkoxycarbonyl, etc.; a proviso is given; R3 = H, alkyl, etc.; ring E1 = unsatd. heterocyclic ring, etc.; ring E2 = unsatd. heterocyclic ring, etc.; ring E3 = unsatd. or satd. heterocyclic ring, etc.; ring E3 may be omitted; ring E4 = unsatd. heterocyclic ring, etc.; R4, R5 = CO2R8, etc.; R8 = H, alkyl, etc.; p, q = 0, or 1, 2; p + q = 1 or 2; R6, R7 = H, alkyl, etc.; m = 1 - 3; n = 1 - 3] are prepd. I are useful as preventives and/or remedies for various vascular lesions assocg. accelerated coagulation activity, for example, universal intravascular coagulation syndrome, coronary thrombosis, brain infarction, brain embolism, transient cerebral ischemic attack, diseases assocg. cerebral vascular disorders, deep vein thrombosis, peripheral embolism, thrombus formation following artificial blood vessel operation or artificial valve replacement, diseases assocg. postoperative thrombus formation, reobstruction and reconstriction following coronary artery bypass, reobstruction and reconstriction following PTCA or PTCR, thrombus formation during extracorporeal circulation and glomerulonephritis. Formulations contg. a compd. of this invention are given. In an in vitro test, 2-[2-(4-amidinophenylcarbamoyl)-6-methoxy-3-pyridyl]-5-[(1(S)-hydroxymethyl-2,2-dimethylpropyl)carbamoyl]benzoic acid methanesulfonic acid salt showed IC50 of 0.013 .mu.M against factor VIIa.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 1998:550423 CAPLUS
DN 129:175969
TI Preparation of .beta.-(arylcarbonylamino)alanines and analogs as fibrinogen receptor antagonist prodrugs
IN Egbertson, Melissa S.; Young, Steve D.; Hartman, George D.; Cook, Jacquelynn J.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 78 pp.

CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9834935	A1	19980813	WO 1998-US1998	19980202
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RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9861413	A1	19980826	AU 1998-61413	19980202
AU 747293	B2	20020516		
EP 1023295	A1	20000802	EP 1998-906092	19980202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2001512439	T2	20010821	JP 1998-534824	19980202
US 5981584	A	19991109	US 1998-23650	19980203
PRAI US 1997-36901P	P	19970206		
GB 1997-7489	A	19970414		
WO 1998-US1998	W	19980202		

OS MARPAT 129:175969
AB H2NC(:NOH)Z1Z2Z3CONHCH2CR2R3CO2R4 [I; R2,R3 = H, OH, CO2H, (un)substituted amino, etc.; R4 = H, alkyl, aryl, etc.; Z1 = (un)substituted phenylene; Z2 = (CH2)mZ(CH2)p; Z = bond, O, CO, NH, CONH, etc.; Z3 = heterocyclylene, (hetero)arylene, etc.; m,p = 0-6] were prepd. as fibrinogen receptor antagonist prodrugs (no data). Thus, 4-(NC)C6H4NO2 was etherified by 4-(HO)C6H4CO2H and the product amidated by (R)-H2NCH2CH(CO2Et)NHSO2C6H4Me-4 to give, after oximation, (R)-I (R2 = H, R3 = NHSO2C6H4Me-4, R4 = Et, Z1 = Z3 = 1,4-phenylene, Z2 = O).
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 1995:998406 CAPLUS
DN 124:203098
TI Preparation of peptide factor Xa inhibitors as antithrombotics.
IN Al-Obeidi, Fahad; Lebl, Michal; Ostrem, James A.; Safar, Pavel; Stierandova, Alena; Strop, Peter; Walser, Armin
PA Selectide Corp., USA
SO PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9529189	A1	19951102	WO 1995-US5268	19950425
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, UZ, VN				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2186497	AA	19951102	CA 1995-2186497	19950425
AU 9523683	A1	19951116	AU 1995-23683	19950425
AU 707653	B2	19990715		
ZA 9503361	A	19960112	ZA 1995-3361	19950425
EP 758341	A1	19970219	EP 1995-917736	19950425
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1147261	A	19970409	CN 1995-192811	19950425

	HU 76346	A2	19970828	HU 1996-2954	19950425
	JP 10503477	T2	19980331	JP 1995-527853	19950425
	RU 2152954	C1	20000720	RU 1996-122647	19950425
	EE 3973	B1	20030217	EE 1996-146	19950425
	IL 113505	A1	19991231	IL 1995-113505	19950426
	TW 409129	B	20001021	TW 1995-84104681	19950511
	FI 9604317	A	19961025	FI 1996-4317	19961025
	NO 9604553	A	19961227	NO 1996-4553	19961025
	LT 4218	B	19970925	LT 1996-151	19961025
	LV 11740	B	19971220	LV 1996-410	19961115
	US 5849510	A	19981215	US 1997-947794	19971008
PRAI	US 1994-233054	A	19940426		
	US 1995-428404	B1	19950425		
	WO 1995-US5268	W	19950425		

OS MARPAT 124:203098

AB A1-A2-(A3)m-B [m = 0, 1; A1 = R1-R2-R3; A2 = R4-R5-R6; A3 = R7-R8-R9; R1 = (substituted) 1-20 amino acid residues, R11CO, R11R12X; X = N, CH, NCO; R11, R12 = H, alkyl, acyl, aryl, aralkyl, protecting group; R2 = CR99R100; R99, R100 = H, (substituted) alkyl, aralkyl, heteroaralkyl, heteroaryl; R3 = CO, CH2, CHR99CO, etc.; R4 = CH2, imino; R5 = CR201R202; R201, R202 = H, (substituted) alkyl, aryl, aralkyl; R6 = CO, CH2, CHR99CO; R7 = (substituted) R4; R8 = CR210R211; R210, R211 = H, (substituted) alkyl, alkylaryl, heterocyclyl; R9 = CO, CH2, CHR99CO; B = (substituted) 1-20 amino acid residues, amino, OH, alkoxy, acyloxy, etc.; with provisos], were prepd. Thus, Ac-Tyr-Chg-Arg-NH2 (Chg = cyclohexylglycyl) inhibited coagulation in human plasma with EC50 = 2.5 .mu.M.

L11 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2003 ACS

AN 1982:103923 CAPLUS

DN 96:103923

TI Semisynthetic cephalosporins with .alpha.-oximino acid side chains. The preparation and coupling of 4-acylamino-.alpha.-oximinobenzeneacetic acids and 1,2-dihydro-6-methyl-.alpha.-oximino-2-oxo-3-pyridineacetic acid to 7-aminocephalosporanic acid

AU Domagala, John M.; Haskell, Theodore H.; Showalter, H. D. Hollis

CS Chem. Dep., Warner-Lambert, Ann Arbor, MI, 48105, USA

SO Journal of Antibiotics (1981), 34(11), 1447-55
CODEN: JANTAJ; ISSN: 0021-8820

DT Journal

LA English

AB A series of 4-acylamino-.alpha.-oximinobenzeneacetic acids, and 1,2-dihydro-6-methyl-.alpha.-oximino-2-oxo-3-pyridineacetic acid were prepd. and coupled to 7-aminocephalosporanic acid and its 3-(1-methyltetrazol-5-yl)thio analog. Several coupling methods and oxime protecting groups were thoroughly examd. The best coupling procedure employed Me2N+:CHClCl-, and the tetrahydropyranyl group was selected for oxime protection. The cephalosporins prepd. were active against Staphylococcus aureus, but less effective than cefuroxime and cefotaxime. The corresponding .alpha.-keto acids, and O-Me oximes were less active.

L11 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2003 ACS

AN 1981:83728 CAPLUS

DN 94:83728

TI Synthesis of (Z)-4-(acylamino)- and 4-(alkylamino)-.alpha.-oximinophenylacetic acids: properties and stereochemical determination

AU Domagala, John M.; Haskell, Theodore H.

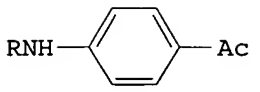
CS Chem. Dep., Warner-Lambert/Parke-Davis Pharm. Res. Div., Ann Arbor, MI, 48105, USA

SO Journal of Organic Chemistry (1981), 46(1), 134-40
CODEN: JOCEAH; ISSN: 0022-3263

DT Journal

LA English

GI



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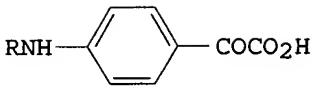


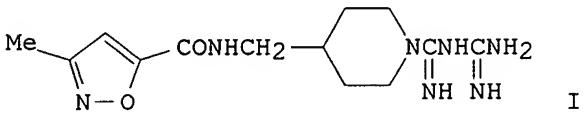
II

AB Acetophenones I (R = Ac, PhCH2O2C) were oxidized by SeO2 to give phenylglyoxylic acids II, which were converted to their corresponding oximes. The stereochem. of these oximes was detd. to be Z (syn.).

AN 1979:593292 CAPLUS
DN **91:193292**
TI 1-(N-Amidino)amidino-4-N-(3-methyl-5-isoxazolylcarbonyl)aminomethylpiperidine sulfate
IN Honna, Koji; Hashimoto, Sadao; Suzue, Takashi
PA Taiho Yakuhin Kogyo K. K., Japan
SO Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 54066685	A2	19790529	JP 1977-132813	19771105
	JP 62005156	B4	19870203		
PRAI	JP 1977-132813		19771105		

GI



I

AB Refluxing 3.5 g Me 3-methylisoxazole-5-carboxylate with 5.7 g 4-(aminomethyl)piperidine in MeOH 7 h and treating with HCl gave 67.8% 4-[N-(3-methyl-5-isoxazolylcarbonyl)amino]methylpiperidine-HCl, which (8.4 g) was heated with 2.8 g H2NC(:NH)NHCN 1 h at 150-60.degree. to give, after converting to the sulfate, 42.1% I.0.5H2SO4. I is useful as a hypoglycemia and hypolipemic agent (no data).

=> analyze l1
ENTER ANSWER NUMBER OR RANGE (1-):1
ENTER DISPLAY CODE (TI) OR ?:rn
L2 ANALYZE L1 1 RN : 5 TERMS

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	14.25	14.46

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.65	-0.65

FILE 'REGISTRY' ENTERED AT 13:27:38 ON 05 NOV 2003

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 3 NOV 2003 HIGHEST RN 612478-18-9
DICTIONARY FILE UPDATES: 3 NOV 2003 HIGHEST RN 612478-18-9

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

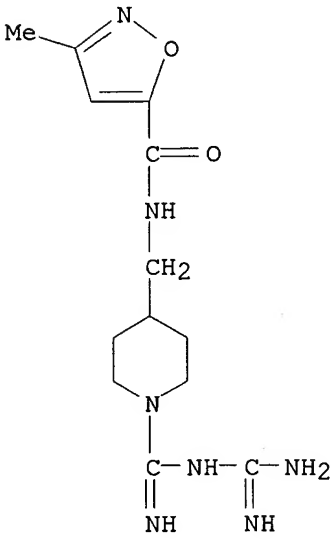
=> s l2
L3 5 L2

=> d 1-5

L3 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2003 ACS on STN
RN **71905-05-0** REGISTRY
CN 5-Isoxazolecarboxamide, N-[[1-[[(aminoiminomethyl)amino]iminomethyl]-4-piperidinyl]methyl]-3-methyl-, sulfate (2:1) (9CI) (CA INDEX NAME)
MF C13 H21 N7 O2 . 1/2 H2 O4 S
LC STN Files: CA, CAPLUS

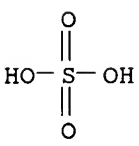
CM 1

CRN 71905-04-9
CMF C13 H21 N7 O2



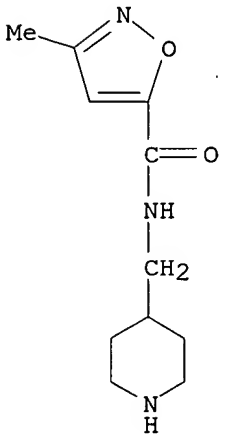
CM 2

CRN 7664-93-9
CMF H2 O4 S



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

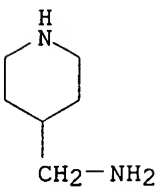
L3 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2003 ACS on STN
RN **71905-03-8** REGISTRY
CN 5-Isoxazolecarboxamide, 3-methyl-N-(4-piperidinylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)
MF C11 H17 N3 O2 . Cl H
LC STN Files: CA, CAPLUS

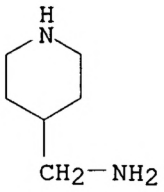


● HCl

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2003 ACS on STN
RN **7144-05-0** REGISTRY
CN 4-Piperidinemethanamine (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Piperidine, 4-(aminomethyl)- (7CI, 8CI)
OTHER NAMES:
CN 4-(Aminomethyl)piperidine
CN NSC 194294
CN NSC 62826
FS 3D CONCORD
MF C6 H14 N2
CI COM
LC STN Files: BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CSCHEM, HODOC*, IFICDB, IFIPAT, IFIUDB, SPECINFO, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)




H
N
CH2—NH2